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CONTENTS OF VOLUME XVI

JULY, 1918. NUMBER 1

PAGE

A New Microbody Found in the Blood in a Case of Myelogenous Leukemia, and the Efficacy of Arsphenamin on the Disease. Itsuyoshi Imaba, M.D., and Shin Ohashi, Mukden, South Manchuria 1

A Clinical Consideration of Macewen's Sign, Especially with Reference to Its Use in Poliomyelitis. Joseph G. Regan, M.D., Brooklyn 13

The Curative and Prophylactic Value of Vaccines in Pertussis. L. H. Barenberg, M.D., New York 23

Further Report on the Use of Pertussis Vaccine Controlled by the Complement Fixation Test. E. J. Huenekens, A.B., M.D., Minneapolis 38

A Protective Therapy for Varicella and a Consideration of Its Pathogenesis. Alfred F. Hess, M.D., and Lester J. Unger, M.D., New York 34

Energy Metabolism of an Amaurotic Family Idiot. Fritz B. Talbot, M.D., Boston 39

A Combined Temperature, Weight, Food, Symptom, Etc., Record Chart for Pediatric Work. H. J. Gerstenberger, M.D., and H. O. Ruh, M.D., Cleveland 44

Is the Amount of Calcium Usually Given in Dilutions of Cow's Milk Injurious to Infants? L. Emmett Holt, M.D., Angelia M. Courtney and Helen L. Fales, New York 52

Current Pediatric Literature 57

AUGUST, 1918. NUMBER 2

PAGE

Neoplastoma Sympatheticum. S. Burt Wolbach, M.D., and John Lovett Morse, M.D., Boston 63

Variation in the Lipoid ("Fat") Content of the Blood of Infants under Certain Nutritional Conditions. W. McKim Marriott, M.D., St. Louis, and Warren R. Sisson, M.D., Boston 75

Active Immunization of Infants Against Diphtheria. Abraham Zingher, M.D., D.P.H., New York 83

Infantilism, with Two Cases of the Brissaud and the Frölich Types, Respectively. J. P. Crozer Griffith, M.D., Philadelphia 103

Intrathecal Injection of Horse Serum in the Treatment of Chorea. Langley Porter, M.D., San Francisco 109

Breath Holding in Infants. Isaac A. Abt, M.D., Chicago 118

Balantidium Coli Infection with Report of a Case in a Child. L. R. DeBuys, B.S., M.D., New Orleans 123

Current Pediatric Literature 130

American Journal of Diseases of Children

Vol. 16 SEPTEMBER, 1918 No. 3

IMMUNITY REACTIONS IN HYDRATED AND CONCENTRATED TISSUE *

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That certain types of organisms succumb more readily to the invasion of disease than others is an old clinical observation. This gradually crystallized into the expression that the apparently fat, plethoric organism showed on the whole a lesser degree of resistance than the lean, fairly emaciated organisms. This experience is quite strikingly borne out in two familiar disease processes; the pneumococcus infection and tuberculosis.

If one will look on certain types of obese organisms as having tissue with a larger water content than the thin, lean organism one may use the expression that in the former case we are dealing with hydrated tissue and in the latter case with concentrated tissue. That hydration or concentration of tissue bears some definite relationship to immune reactions unfavorable in the hydrated and favorable in the concentrated tissue is a thought which has repeatedly been expressed in the literature.

REVIEW OF THE LITERATURE

Among pediatrists, Czerny[1] and his followers have mentioned the possibility of this connection and have published some interesting observations bearing on the point. Czerny emphasizes the connection existing between a state of nutrition and the natural immunity of an organism, and states in fact, that natural immunity is dependent on the state of nutrition. He points out that there are differences between the natural immunity of different tissues and organs and explains in this way the localization of infectious disease processes.

Congenital factors can affect the development of immunity as well as changes wrought during the advancing age of the tissue.

Czerny finds that natural immunity is least developed in the premature, very slightly during the first few years, and shows a maximum

* Submitted for publication, July 1, 1918.
* From the Department of Pediatrics and Bacteriology and Pathology, University of Minnesota, and the Minneapolis City Hospital.
* Read at the Annual Meeting of the American Pediatric Society, Lenox, Mass., May, 1918.

1. Czerny, A.: Med. Klin., 1913, No. 23, p. 895.

development during adolescence and middle age. From clinical experience he comes to the conclusion that the infant who can tolerate the largest amount of fat in his food shows the best natural immunity. High carbohydrate feeding while generally well tolerated, lowers immunity to an unusual degree. Infants with a higher water content in the tissues are very vulnerable to infection. Premature and newly born infants are easily infected. There is little tendency to localization. The infection quickly becomes general. The infection with tuberculosis, for example, is a striking instance.

In this connection the experimental work of Weigert[2] on young pigs infected with tuberculosis is interesting. He found that the pigs fattened on high carbohydrate feeding whose tissues were in a state of hydration, as it were, showed an exceptionally low resistance to the infection as compared with normal pigs or those fed on mixtures predominating in fat content. Weigert believes that there is a definite connection between natural resistance and the water content of the tissues. It is probably one of a series of biologic physical or chemical factors which influence or modify the constitution of the organism and on which immunity depends.

The laws governing the behavior of the water content of the tissues of various animal species are today still the same as those expressed and formulated by V. Bezoldt[3] over fifty years ago. Every individual animal organism has a content of water, organic material and inorganic salts, typical for its age and species. This is either nearly constant or it may vary between wide degrees.

The growth and development of every animal is characterized by changes, typical for each species, in the composition of the above named components. These changes are principally:

(a) Decrease in the organism of water and volatile components from the embryonal stage until the period of free growth.

(b) Increase in content of solid inorganic material. This increase being particularly rapid for the first period after birth.

(c) A steady growth, although extremely slow during the first period of life, of the ash content. This growth continues until the completion of the period of progressive development.

Weigert's[4] experiments confirmed generally the above laws. He concludes that the water content of the animal's tissue depends on its age and nutrition. Variations of the water content are not alone determined by increase or decrease of the fat content of the animal organism, but are also determined by a varying content of fat-free,

2. Weigert, R.: Berl. klin. Wchnschr., 1907, No. 23, p. 1209.
3. Bezoldt, V.: Ztschr. f. Wissenschaftl. Zool., 1857, **8,** 487.
4. Weigert, R.: Jahrb. f. Kinderh., 1905, **61,** 178.

dry substance. The increase of fat-free, dry substance involves equally the content of nitrogen and ash. Animals fed on protein and fat-rich food show the largest content of fat-free, dry substance. Applying his results to the infant organism, Weigert concludes that the breast-fed infant's organism has a lower water content than the artificially fed on account of the greater fat percentage of breast milk.

The coincidence of diminished water content of the organism with increased resistance to infection explains the natural immunity of the breast-fed infant. The question here might be raised whether this is the only factor operative in this higher degree of resistance. It is now a known fact that immune bodies can pass from the mother to the nursing offspring through the breast milk.

R. Lederer,[5] studying the relationship of water to constitution and nutrition, reports the interesting finding that one-sided feeding of young animals on cow's milk, dogs in this case, caused the normal, physiologic dehydration of the growing organism to remain stationary, or even could cause increase in the water content of the blood. Excessive intake of fluid along with other food could delay the drying out of the organism. The same thing could be accomplished by continuing breast feeding beyond the physiologic period of weaning. Lederer finds that the curve of physiologic dehydration shows an abrupt interruption shortly after birth. The water content of the blood of the new-born increased from birth until about the middle of the third month. From this period on, the slow physiologic dehydration continues to adolescence.

These findings are of some interest in connection with the view expressed by Czerny in reference to immunity in the young, under conditions of natural and artificial feeding. A part phenomenon of natural immunity is the capability of the organism to react to an infection with the formation of specific immune bodies. Most of the recent experimental work has for this reason been along immunologic lines, and has concerned itself with a search for these immune bodies and with a study of their behavior under varying conditions.

Moro[6] found complement in the serum of the fetus and the new-born in an amount virtually equal to that of the adult. In the breast-fed infant it reaches this amount as early as the fourth or fifth day, and remains quite constant. The conditions are much the same in the artificially fed infant, except that there are variations in the amount and frequently diminution. He found the complement content of the atrophic infant and those suffering from alimentary disturbances far below the normal, and found that it could be markedly influenced by nutrition.

5. Lederer, R.: Ztschr. f. Kinderh., 1914, **10,** 365.
6. Moro, E.: Monatschr. f. Kinderh., 1907, **6,** 340.

Adair[7] found hemolytic complement in the new-born babe and could demonstrate it in fetuses as early as the eighteenth week of fetal life. It was present in smaller amounts in the fetal than in the maternal serum. He concludes from his experiments that the hemolytic complement is developed in the fetal blood and that the amount developed is controlled by the fetal organism.

Heiman[8] found the actual and potential complement content of the blood reduced in the artificially fed infant. Kaumheimer[9] could not corroborate the findings of Moro, but found the complement content high in the organism favored with an apparently normal constitution, but distinctly lower in the organism with abnormal constitutional manifestation.

E. Thomas[10] and O. Horneman[11] carried out a series of experiments on pigs analogous to those reported by Weigert in this case, however, determining the immune reactions on young pigs infected with tuberculosis and subjected to various feeding conditions. These observers found that pronounced variation in the feeding had no influence on the complement content or the opsonic index. Both the infected and noninfected animals showed no difference in the complement content. They corroborated the findings of Weigert that high protein feeding retarded the spread of the infection whereas high carbohydrate feeding favored it.

Kleinschmidt[12] studied the antibody formation on young dogs under both natural and artificial feeding conditions. Hemolysis and agglutination were the reactions principally determined. He found that neither high carbohydrate nor high fat content of the artificial food influenced antibody formation to any degree. Alimentary disturbances, however, can hinder antibody formation. Marked disturbance of the antibody formation occurring during an alimentary disturbance can quite rapidly be brought back to normal during the repair stage if the animal is placed on natural feeding. During the repair stage, for example, the hemolysis can be practically normal, even if the body development is markedly retarded. Kleinschmidt concludes from his experiments that the constitution of the organism is more important by far for the development of immune reactions than is the type of feeding.

P. T. Müller[13] studied the influence of artificially produced alter-

7. Adair, F. L.: Tr. Am. Gynec. Soc., 1915.
8. Heiman: Monatschr. f. Kinderh., 1907, **6,** 340.
9. Kaumheimer, L.: Centralbl. f. Bakteriol., 1909, **49,** 208.
10. Thomas, E.: Biochem. Ztschr., 1913, **57,** 456.
11. Horneman, O.: Biochem. Ztschr., 1913, **57,** 473.
12. Kleinschmidt, H.: Monatschr. f. Kinderh., Ong. 1914, **12,** 423.
13. Müller, P. T.: Arch. f. Hyg., 1904, **51,** 365.

ations in the metabolism on the production of antibodies. One series of doves was fed on food rich in fat and protein, and a second series on food rich in carbohydrate and deficient in protein and fat. The animals were then subjected to infection with different types of organisms. He could not show definitely that the type of feeding had any consistent influence on antibody production. For some organisms it was marked, for others not. Much seemed to depend on the nature of the micro-organism that was used as the infecting agent.

Trommsdorff[14] studied factors which would tend to reduce the natural resistance of the organism to infection. His work was carried out on guinea-pigs. In connection with the present study his results from the effect of starvation on production of immune bodies are particularly interesting. Trommsdorff comes to the conclusion that starvation has an unfavorable influence on the production of antibodies. Prolonged periods of hunger would, for example, diminish hemolysis or abolish it altogether.

Similar results were found by Bakunin and Boccardi[15] who found the alexin content of the blood of starving dogs and doves reduced or absent. Meltzer and Norris,[16] on the other hand, did not find that the bactericidal faculty of the blood serum of starved dogs was decreased. Rosatzin[17] found no change in this respect in rabbits deprived of food and water. Roger and Josue,[18] and Teissier and Guinard[19] observed that withdrawal of food paramount to starvation would at first lessen the animal's organism resistance to infection. If the starvation, however, was not carried to extremes and was continued over a long period, the animals were found to be much more resistant than the control animals.

AUTHOR'S EXPERIMENTS

The work I wish to report was undertaken to show whether there was any difference in the defensive mechanism of hydrated or concentrated tissue, using determinations of immune reactions as an index.

Parallel series of guinea-pigs were taken, as near as possible in age and weight for each series. The animals were kept under the best conditions possible. The preliminary feeding stage covered a considerable period before immunization. In the fat series, the attempt was made to cause increase in weight as rapidly as possible through

14. Trommsdorff, R.: Arch. f. Hyg., 1906, **59,** 1.
15. Bakunin and Boccardi: Riforma med., 1891, No. 188.
16. Meltzer and Morris: Jour. Exper. Med., 1899, **4,** 131.
17. Rosatzin: In Lubarsch. Zin Lehre von den Geschwulsten in Infect. Krank., Weisbaden, 1899.
18. Roger and Jossué: Semaine méd., 1900, No. 29, p. 235; Compt. rend. Soc. de Biol., 1900, **52,** 696.
19. Teissier and Guinard: Semaine méd., 1897, p. 67.

the use of liberal carbohydrate feeding, particularly maltose. The weight increase occurs rapidly if the pigs are kept under favorable conditions. Some allowance must, of course, be made for normal growth. The lean series of pigs were kept on a balanced ration just sufficient to sustain them. The development of scurvy was prevented by the use of moderate amount of fresh vegetable matter. The weight loss was brought about gradually and, before immunization, generally amounted to from 25 to 35 per cent. of the original body weight. The pigs were sound and active and showed no external evidence of disease. On account of the difficulty at present in obtaining material, the series tested for agglutination was on a shorter preliminary feeding period than the animals used in the other series.

The lysin reaction was compared in fifteen fat animals and eighteen lean animals. The animals were immunized against blood cells by intraperitonal inoculations. About one-fourth c.c. of washed blood cells were injected intraperitoneally at from two to three day intervals. Two weeks following the third or fourth injection the animals were exsanguinated, the blood allowed to clot, and then centrifuged in order to separate the serum from the clot. The serum was then diluted with salt solution 1 : 10, and its lytic titer determined in the usual way. Objections might be made to this method on the ground that the serum of various guinea-pigs may not have contained the same amount of complement. It is a known fact that complement and amboceptor may replace each other within certain limits. However, it seemed that this was a more accurate method than to inactivate the serum in order to destroy the complement, as in the operation of inactivation, an appreciable quantity of antibodies is destroyed.

The precipitin reaction was carried out on eleven fat and eleven lean animals. The animals were treated with from one-fourth to one-half c.c. of ascitic fluid or human blood serum intraperitoneally as was done with the lysin pigs. The precipitin titer of the serum was then determined by the dilution method.

The agglutination was determined in seven fat and seven lean animals. The procedure was much the same as in the precipitin reaction. Pigs were inoculated intraperitoneally with a twenty-four hour killed culture of the typhoid bacillus. Four injections were made at three or four day intervals. Ten days following the last injection the titer of the serum was determined by the dilution method.

RESULTS

From the accompanying tables it can be seen that the lysin reaction was negative or nearly so in practically all of the fat animals, but was positive, sometimes to a marked degree, in over 60 per cent. of the

TABLE 1.—Comparative Results of the Experiments Undertaken to Determine the Lysin Reaction

Fat Animals (High Carbohydrate Feeding) (Immunized with Sheep Cells)				Lean Animals (Balanced Ration) (Immunized with Sheep Cells)			
	Initial Weight, Gm.	Final Weight, Gm.	Hemolysis		Initial Weight, Gm.	Final Weight, Gm.	Hemolysis
Series I				Series I			
Pig 1	280	630	0.08	Pig 13	250	190	0.04
2	355	840	No hemolysis	14	335	200	0.06
3	320	865	0.06	15	305	185	0.06
4	270	665	0.08	16	275	195	0.08
5	300	870	0.06	17	315	210	0.08
6	310	785	0.08	18	295	185	0.06 partial 0.05
Series II				Series II			
Pig 25	400	700	complete 0.06 partial 0.04	Pig 30	480	310	0.04
27	375	780	complete 0.1	32	435	350	0.06
28*	405	615	complete 0.04				
Series III				Series III			
Pig 40	345	825	No hemolysis	Pig 41	460	365	0.08
43	425	920	0.08	42	395	250	0.06
45	450	940	0.06	48	360	250	0.08
59	395	985	0.08	49	405	295	No hemolysis
				60	400	290	0.02
				61	415	325	0.04
Series IV				Series IV†			
Pig 52	265	655	0.08	Pig 54	335	350	0.08
53	270	600	0.08	55	450	515	0.06
				57	390	370	0.08
				58	400	385	0.06

* Pig had lost 235 gm. in past two weeks.
† Stationary weight.

TABLE 2.—Results Obtained in Determining the Precipitin Reaction

Fat Animals (High Carbohydrate Feeding) (Immunized with Ascitic Fluid)				Lean Animals (Balanced Ration) (Immunized with Ascitic Fluid)			
	Initial Weight, Gm.	Final Weight, Gm.	Precipitation		Initial Weight, Gm.	Final Weight, Gm.	Precipitation
Series I				Series I			
Pig 7	350	910	—	Pig 19	275	180	—
8	265	595	—	20	300	195	—
9	250	740	—	21	280	190	—
10	280	635	slight	22	305	185	slight
11	300	825	—	23	295	200	—
12	280	710	—	24	310	195	—
Series II				Series II			
Pig 33	385	635	trace, layer test	Pig 37	395	310	—
34	300	670	—	39	415	250	—
(Immunized with Human Serum)				(Immunized with Human Serum)			
Series III				Series III			
Pig 44	380	750	slight	Pig 50	415	250	—
46	610	1,035	—	51	435	385	—
47	435	830	—	62	390	295	—

lean pigs. The precipitin reaction was uniformly negative in both the fat and lean series. For some unaccountable reason the guinea-pig serum does not give the precipitin reaction. This is strange in view of the behavior of the agglutinin reaction, which while present in only 11 per cent. of the fat animals, was positive in over 70 per cent. of the lean animals. To draw far reaching or final conclusions from a study of this kind is surely unwarranted.

If, however, immunity reactions are a good criterion of tissue resistance the rather striking behavior of both the lysin and agglutinin reaction would seem to indicate that there is a difference in favor of concentrated tissue and that the theoretical considerations expressed by Czerny and other observers are substantially correct.

The author wishes to acknowledge the valuable assistance and helpful suggestions of Dr. W. P. Larson of the Department of Bacteriology and Pathology in the University of Minnesota.

CONGENITAL ATRESIA OF THE ESOPHAGUS

WITH REPORT OF FOUR ADDITIONAL CASES, WITH THREE NECROPSIES *

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CHICAGO

In 1913 I[1] reported three cases of congenital atresia of the esophagus with necropsies which I had seen within a period of one year. In two succeeding years four additional cases have come under my observation. In my own experience no other congenital anomaly of the intestinal tract has approximated even remotely so great a number with the possible exception of hyperplastic stenosis of the pylorus. Among my colleagues (Drs. Richter, Grulee, Hess, Michael, Jackson and others) I have knowledge of at least six or seven more cases. In all of these cases there was identically the same clinical and anatomic picture. In all of them the upper end of the esophagus ended blindly, the lower end connected the stomach with the trachea — the so-called "inosculating" type of atresia of the older writers.

In 1884 Sir Morrell Mackenzie[2] collected 62 cases of congenital atresia of the esophagus and added one of his own. He placed the incidence of the "inosculating" type at about 70 per cent. In 1905 Kreuter[3] collected 98 cases, in only 64 of which it was reported that the esophagus was connected with the trachea, or a bronchus (65 per cent.). Cautley[4] in a recent (1917) somewhat less complete summary gives a detailed classification of type incidence of all congenital malformations of the esophagus, with a report of 85 cases of atresia, with about the same percentage of cases in which there was a connection between trachea and stomach as in the former reports.

My associate, Dr. W. Stanley Gibson, recently made an exhaustive search of all the literature on this condition. A full report of this review of the literature would detract attention from the main point of this short clinical paper, that is, that one type of atresia occurs with stereotyped regularity. Gibson found that since Kreuter's[3] sum-

* Submitted for publication June 20, 1918.

1. Brennemann, Joseph: Congenital Atresia of the Esophagus, with Report of Three Cases, Am. Jour. Dis. Child., 1913, **5**, 143.

2. Mackenzie, Sir Morrell: Manual of Diseases of the Throat and Nose, 1884, **2**, 216.

3. Kreuter: Die Angeborenen Verengungen und Verschliessungen des Darmkanales im Lichte der Entwickelungsgeschicte, Habilitationsschrift, Erlangen, 1905.

4. Cautley, Edmund: Malformation of the Esophagus, Brit. Jour. Dis. Child., 1917, **14**, 1.

mary, in 1905, some twenty or twenty-five cases have been reported, *all of which have been of the type here reported.* It is evident that in these cases there is a definite developmental anomaly that regularly follows a certain course, the exact nature of which is still in dispute and lies beyond our present discussion. Since practically all of the cases in the more recent and more exact reports have belonged to this one type, it has seemed to me worth while to report these further cases that exemplify this unity of type, and to emphasize the fact that for all practical diagnostic and therapeutic purposes congenital atresia of the esophagus is one definite clinical and anatomic complex.

The peculiar variation in the frequency with which these cases occur in the experience of different reporters suggests a further motive. Shukowsky and Baron[5] reported a case in 1912, the only one on record in a hospital experience of 50,000 new-born infants. The English pediatrician Cautley[4] reported a case in 1917, the first he had seen in "25 years of practice, mainly among children," and that " in the child of a Belgian refugee." Hirschsprung,[6] on the other hand, saw, and later reported, four of these cases within seven months while assistant surgeon in the Lying-in Hospital in Copenhagen, and reported five other cases, "two placed at his disposal by his chief, Professor Levy, one from the archives of the hospital," and two more observed later. Lotz[7] reported eight cases, specimens of which he found in the Pathological Institute at Giessen, and three of which had been reported previously.

The heaping of these cases in my own experience may serve as a further example. It is a very common occurrence in practice that a clinician who sees a rare case becomes interested in finding others and is soon rewarded in his search. It seems not unlikely that many more of these cases occur than are diagnosed. Possibly infants that have died in the first week or two of life because they were unable to retain food, or were erroneously reported as "vomiting everything," without showing evidence of pyloric or other well known obstruction, may have belonged in this category, and being only babies, who are supposed to do such things, have not been permitted even the consolation of an exact diagnosis. The diagnosis is singularly easy to any one who has the condition in mind or has ever seen a case. A colleague in a neighboring city recently sent me a reprint of his report of a case of the regular type which he had seen and necropsied, with

5. Shukowsky and Baron: Arch. f. Kinderh., 1912, **58,** 191.

6. Hirschsprung, H.: Den Medfodte Tillerkning of Spieseröret, Inaug. Dissert., Copenhagen, 1861. Also, Cases of Congenital Atresia of the Esophagus, Hospitalstid., 1895, Part 4, **3,** 1037.

7. Lotz: Ueber die Kongenitale Atresia der Spieserohre, Giessen, 1910.

the comment, "This was the first case I saw after I got home from the Clinical Pediatric Congress in Chicago," where I had been fortunate enough to be able to demonstrate a living case. For this further reason I hope it is not without interest to call attention once more to this apparently not extremely rare condition, although it is regularly rated as such.

Anatomy.—The anatomy of this anomaly is shown in the accompanying figures. The upper end of the esophagus is uniformly dilated to a diameter of about 1 cm. or more, whereas the normal is about 4 to 6 mm., and ends roundly and abruptly at, or within, a centimeter above the level of the bifurcation of the trachea. The lower end of the esophagus is of approximately normal diameter, or slightly lessened. It runs directly from its normal location at the cardiac end of the stomach into the posterior aspect of the trachea at, or somewhat above, the bifurcation, or in a few cases it has been reported ending in a bronchus. This portion is usually from 4 to 7 cm. in length and commonly tapers slightly toward the tracheal end. In many cases it has been reported that a strand of dense "fibromuscular" tissue connected the lower end of the upper portion with the upper end of the lower portion. Thus Lotz[7] reports two such cases out of the eight that he reported. Others have reported a much higher ratio. The presence or absence of such a band is not always easy to determine, and little reliance can be placed on the published summaries with reference to this point.

Symptoms.—The symptomatology is strikingly uniform. An infant that in no way attracts interest to itself, pathologically, begins very quickly to unfold a series of symptoms that are pathognomonic and that could be predicted from a knowledge of the anatomic conditions. If the baby receives no food or water for some time after birth the first symptom is a constant slight flow of saliva from the more dependent corner of the mouth. If it is now put to the breast, or is given water it will swallow once or twice without any trouble. With every further attempt at swallowing the fluid will return in jets alongside of the nipple and through both nostrils. The child is now compelled to breathe with the mouth, nose and pharynx full of liquid. It suddenly stops nursing, its eyes become fixed, it rapidly turns blue and then struggles to empty its lungs by coughing. This is only gradually successful, and during this time it becomes deeply cyanotic, almost black. If it is not relieved either by its own efforts or by those of an attendant, it ceases to struggle, becomes quiet, stops breathing and is evidently drowning. Such an end seems relatively rare and is apparently a real danger only as the child gets very weak. If fluids are still

given, unwisely, after the diagnosis is made, the baby will often toward the end make almost no attempt to empty the lungs, will simply become quiet and relaxed, stop breathing, become cyanotic and give up without a struggle. Probably in all stages some, and, at times, nearly all of the fluid that enters the lung escapes by way of the lower portion of the esophagus into the stomach, and this is doubtless another factor that makes immediate death from drowning so rare. The return to normal is greatly hastened at any stage by lifting the baby by the feet to an almost vertical position with the face downward so that the inhaled fluid can run out. After this has been accomplished it lies quiet and exhausted for some time, only to repeat the whole cycle again with each new attempt at nursing. It has been said that these attacks of suffocation occur independently of nursing, as a result of the vomiting of fluid from the stomach into the trachea through the lower portion of the esophagus. This has not been my experience except after gastrostomy, when fluid poured into the stomach for obvious reasons produces the same symptoms as when taken by mouth.

If milk has been taken it is mixed with the mucus from the nasopharynx as it is expelled and is whipped by the respired air into a fine whitish froth at the nares.

The stomach is slightly distended with air while the rest of the abdomen is flattened. This symptom has been present in every one of my cases and is important, as it establishes the fact that the stomach and trachea are connected.

For a few days the stools are normal in amount and are typical meconium. They then become scant, or absent, and if present are the typical greenish-brown slimy stools that characterize starvation.

After the second or third day there is an inanition temperature of moderate degree. This may persist throughout, or the temperature may become normal, or subnormal; it may or may not again rise as the aspiration or terminal bronchopneumonia that is always found at necropsy makes its advent.

The infant becomes rapidly weaker and more apathetic. Emaciation at first is rapid, then more slow, with a final loss of 25 per cent. to 40 per cent. of weight, depending on how long the child lives. The fontanel becomes depressed, the tissues dry and boardlike; the skin is drawn tightly over the hardened subcutaneous tissue, from which it can no longer be separated; the limbs are stiff; the face is drawn and fixed like a mask; the breathing becomes shallow and almost imperceptible; the cry becomes faint, high pitched and finally absent; the whole child resembles an automaton more than a living thing. Death is commonly so gradual that the time at which it takes place can hardly be fixed.

Death always occurs within two weeks. The average duration of life in this series was seven days; the three infants that were not treated surgically and represent more nearly the natural length of life of these cases, lived, respectively, eight, eight and ten days. Practically all of them showed at necropsy a terminal bronchopneumonia, for which conditions are peculiarly favorable here, but which seems to accompany nearly all deaths from marasmus in infancy. I am more inclined to think that the pneumonia is an accompaniment rather than a determining cause of death, and that those infants that are permitted to die naturally all die of starvation from the seventh to the tenth day. None of this series died from suffocation. While the latter form of death is probably wholly avoidable if all mouth feeding is withheld, which is, of course, the only course to pursue after a diagnosis is made, I do not believe that it presents as great immediate danger as observation of an acute attack might lead one to think it would. I am inclined to think that escape of fluid to the stomach through the lower end of the esophagus may be a most important factor in emptying the lungs, especially when the time comes that the baby is not able to expel the fluid through the mouth and nose.

Other congenital anomalies of all kinds are peculiarly frequent in association with atresia of the esophagus. Probably considerably more than half of the cases show one or more such accompanying abnormalities.

Diagnosis.—The diagnosis is very simple if one has the condition in mind, as practically all of the cardinal symptoms are present in each case. The attacks of apparently alarming cyanosis and suffocation when drinking are pathognomonic. The return of fluids from the mouth and nose, synchronous with the act of swallowing and always occurring after at most two swallows, is *sui generis,* and can hardly be mistaken for vomiting if it is seen. If one is sure that a baby has ever taken at one time one-half ounce of fluid by mouth without its immediate return, congenital atresia of the esophagus can be excluded. The flow of saliva from the mouth and the presence of a whitish froth at the nares should alone lead one to the diagnosis. The positive diagnosis as to the upper end of the esophagus is made by passing a sound or catheter. The normal distance of the cardiac end of the stomach from the lips in the new-born is about 17 cm. (Mackenzie[2]). In these cases there is abrupt and unquestionable obstruction to the passage of the sound, with a striking regularity at 12 cm. or a little less. That the lower end of the esophagus connects the stomach and trachea is established by the air-distended stomach.

A detailed description of three cases was given in the former article.[1] On account of the uniformity in all these cases, only brief descriptions of the present four cases will be given.

RREPORT OF CASES

CASE 4.—Baby B. Born on the service of Dr. C. E. Paddock at St. Luke's Hospital; colored; boy; mother had hydramnios; infant's birth weight was 6¼ pounds. The infant was abnormal in many ways: mongolian idiot; eyes not only typical of this condition, but less than one half normal size; palpebral apertures correspondingly small; smaller on left than on right side; ptosis of left eyelid; large toe and only three small toes present on each foot. It had all of the characteristic symptoms of congenital atresia of the esophagus. A sound could be passed only 11.5 cm., stopping abruptly. A slightly distended stomach established the diagnosis of the usual type of atresia. Gastrostomy was done on the sixth day; died four hours later. The infant lost 1¼ pounds in weight, about 25 per cent.

Necropsy.—This was conducted by Dr. A. L. Moody. The upper end of the esophagus was found greatly distended (1.3 cm.) and ended bluntly 4 cm. below the *rima glottidis,* and 1 cm. above the bifurcation of the trachea. The lower end of the esophagus was 6 cm. long and extended directly from the cardiac end of the stomach into the posterior aspect of the trachea 1 cm. above the bifurcation. It was about 4 mm. in diameter. The lower end of the upper and the upper end of the lower portion of the esophagus were at the same level and were connected by a firm connecting tissue.

CASE 5.—Baby E. Service of Dr. H. M. Richter, Wesley Memorial Hospital. Boy. The infant was 3 days old when it entered the hospital. It presented a typical history and appearance of congenital atresia of the esophagus of the regular type. A sound passed 12 cm. The infant died a few hours later, so there are no data as to weight, etc. Operation was performed by Dr. Richter a few hours after it entered the hospital. The technic and *rationale* of a new operation on this case are reported elsewhere by Dr. Richter[8] and will be discussed under treatment.

Necropsy.—The upper end of the esophagus was dilated to 1.5 cm. and ended abruptly 4.5 cm. below the *rima glottidis.* The lower end was 4.5 cm. long, about 5 mm. in diameter, tapering slightly toward the tracheal end, and extended from the cardiac end of the stomach into the posterior aspect of the trachea 5 mm. above the bifurcation. No other anomalies were found, but the examination was lmited to the region in question.

CASE 6.—Baby S. Service of Dr. L. J. Osgood, Wesley Memorial Hospital. Boy. Typical history and clinical findings. The sound stopped abruptly at 12 cm. from the lips; there was a drop in weight from 6 pounds 1½ ounces to 4 pounds, a loss of about 35 per cent.; there was a considerable elevation of temperature throughout after the first day or two. No operation was undertaken. The infant died on the tenth day.

Necropsy.—The anatomic conditions were carefully examined and found exactly as in the other cases. Both specimens and pathologic reports have unfortunately been lost, so that exact measurement and data as to other anomalies cannot be given.

CASE 7.—Baby S. This infant was brought to me by Dr. C. E. Smith of Beloit, Wis., when about 3 days old. Boy; birth weight 7½ pounds. The infant presented all of the typical symptoms. The sound stopped typically at 12 cm. This, together with the moderately air-distended stomach, established the diagnosis of the regular type of atresia. The father was informed of the essentially fatal nature of the condition and of the futility of attempting

8. Richter, H. M.: Congenital Atresia of the Esophagus; an Operation Designed for Its Cure, with a Report of Two Cases Operated on by the Author, Surg., Gynec. and Obst., October, 1913, p. 397.

to relieve it surgically, and readily consented to take it home to let it die as peacefully as possible. The doctor reported later that the baby "died gradually on the eighth day." Necropsy was not permitted. This case was so typical in every way that there can be no doubt that the anatomic relations were the same as in the other cases. I would again emphasize the importance of a *moderately air-distended stomach with an otherwise flattened abdomen* in establishing the fact that the stomach and trachea are connected in a given case.

Fig. 1.—Congenital atresia of the esophagus, posterior view. Case 1, previously reported. The dilated upper end of the esophagus is shown extending from below the rima glottidis to the bifurcation of the trachea; the narrower lower portion from the stomach into the trachea at the bifurcation. Drawn by Miss E. Van Stoesser.

Treatment.—Congenital atresia of the esophagus has always been a fatal disease. Untreated the infants all die in the second week of life of inanition, or of a terminal or aspiration bronchopneumonia that is probably never absent; or, much more rarely, and only, I believe, if mouth feeding is continued, by drowning. Mouth feeding should,

of course, be stopped as soon as a positive diagnosis is made, as it can only hasten the end through suffocation, or aspiration pneumonia. Rectal feeding is wholly inadequate in a new-born infant. At best it can prolong life a very few days.

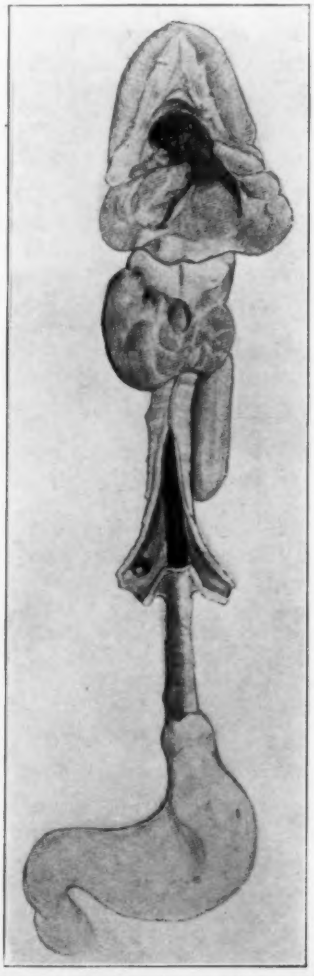

Fig. 2.—Same as Figure 1, anterior view. Upper dilated end of the esophagus partly hidden by the thyroid gland and the trachea. The lower portion of the trachea and the bronchi are laid open showing a sound (black) passing from the stomach through the lower portion of the esophagus into the trachea at the bifurcation. Drawn by Miss E. Von Stoesser.

The problem of treatment is to find some way to feed the child, and one looks to the surgeon for a route.

Surgical procedures have, however, so far served only to end more quickly a hopeless condition. While surgically successful, they

are pediatrically impossible. It is practically impossible to nourish a new-born infant, nearly always already seriously undernourished when the diagnosis is made, when handicapped by the conditions imposed by any of the surgical procedures that have been tried.

Gastrostomy, recommended by Sedillot, has been performed a number of times (Steel, Hoffmann, Happich, Villemin, Kirmisson, Dickie, Demoulin, Richter, Halstead, etc.). In the light of our present knowledge that in practically all of these cases the stomach is freely connected with the lungs, this operation, unless accompanied by closure of the esophagus, no longer finds any justification. Fluids poured in the stomach quickly flood the lungs. The danger of drowning is far more real in this case than in mouth feeding, for in the latter the fluid can escape into the stomach while here it cannot. In fact, it becomes necessary after filling the stomach to hold the child erect and empty the stomach, or death will result. Gastrostomy, alone, is justifiable only if there is no connection between stomach and lungs, and no such case has been reported in over ten years.

Jejunostomy, recommended by Demoulin,[9] and performed by Dr. L. L. McArthur[1] in one of my former cases, would seem sounder, theoretically, at least. The objection again obtrudes itself that a new-born infant so handicapped cannot be nourished sufficiently to maintain life, to say nothing of building it up for a future more radical operation, without which life would be intolerable, even if it were possible. Furthermore, it would seem doubtful whether enough gastric and pancreatic juices that are essential to digestion could find their way into the distal portion of the jejunum, with a lumen so small as that of the small intestine of the new-born and with an opening as large as would be necessary for the introduction of food.

Two attempts have recently been made by H. M. Richter[8] to overcome the objection to the otherwise more serviceable operation of gastrostomy, by closing the upper end of the lower portion of the esophagus, at the same time doing a gastrostomy. The closure of the esophagus must be at the upper end both to save the esophagus for a later radical operation and also to obviate the blind pouch above the point of closure, the contents of which would quickly become dangerously infectious. This necessitates a formidable intrathoracic operation, in addition to the gastrostomy. Richter's[8] technic is given as follows:

> Preliminary gastrostomy under ether. Intubation of lower segment of gullet from below with metal sound. Change to positive pressure ether anesthesia. Incision in left seventh intercostal space, carried upward from posterior

9. Demoulin: Bull. Soc. de chirurgie, July 5, 1904.

end. Five ribs divided near their angles. A silk ligature carried around the gullet, using the sound as a guide. Seventh and eighth ribs brought together by a suture that included both (Sauerbruch). Intrapulmonary tension raised until lung came to chest wall, when remainder of wound was closed. Gastrostomy of the E. J. Senn type now completed and water immediately given through tube.

In the second case practically the same operation was performed, but on the right side instead of the left, as in the former operation. Richter[8] suggests, further, that instead of a simple ligation of the esophagus, "A more definite closure, with separation of the parts, is desirable. The part should be crushed with a heavy clamp, the crushed tissue cut, and both ends turned in." The first child died of shock shortly after the operation; the second child lived twenty hours and received 8 ounces of fluid at short intervals without evidence of flooding of the lungs. In both cases the ligation was successful, as shown in one case by finding the ligature in place at necropsy and in both cases by the fact that there was no suffocation or cyanosis when the stomach was filled.

If this operation can be performed on a new-born infant without death resulting from the operation itself, or from shock, or from infection either from the lower end of the esophagus in the proposed procedure, or from the blind upper end filled with bacteria constantly aspirated into the lungs, or from uncheckable starvation; then it offers some hope that the child can be made to live though always fed through a stomach fistula. The alternative would be a later operation aiming at a restoration of continuity of the esophagus, and the former ligation or separation of the esophagus would seem to add to the difficulty of this herculean task.

The ultimate ideal of all surgical attempts would be this union of the upper and lower portions of the esophagus. It is of interest in this connection that these commonly meet at the same level. Hoffmann[10] attempted this operation, approaching it, however, by the impossible neck route. He gave it up and did a simple gastrostomy, with the inevitable result. Whether this operation will ever be possible the future advances of intrathoracic surgery must decide. Even if possible, it would still seem probable that pediatric limitations will form an insurmountable barrier. In these otherwise hopeless cases, however, one gives the surgeon a full rein with a clear conscience.

When one considers, on the other hand, that nearly all of these infants have other anomalies; that practically all of them either have a bronchopneumonia or will almost inevitably get one if the upper por-

10. Hoffmann: Dissert., Greifswald, 1899.

tion of the esophagus is not drained into the lower portion; that a *restitituo ad integrum* of the esophagus does not yet seem feasible; that without this life, even if possible, would be intolerable; that the child could probably not be made to live even if successfully operated on for pediatric reasons; that no such infant ever has lived, no matter how treated, and finally, that parental sentiment must be weighed heavily in the balance, then if one, after careful counsel with the parents, decides to let the patient die as peacefully and painlessly as possible, one need lose no sleep because of that decision.

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KALA-AZAR IN A CHILD (THE FIRST AMERICAN CASE) *

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History.—K. K., a girl, was born in Greece, Aug. 12, 1912. She entered the Children's Medical Service of the Massachusetts General Hospital, Aug. 15, 1916. Her parents were Greek, and reported that, although they themselves were well, they had lost the first two children, in Greece, of a disease similar to that from which this child was suffering.

The patient came to America in December, 1915. In January, 1916, she had pneumonia, followed by anemia and enlargement of the abdomen. Coincidently, she became weak and listless, and the symptoms became severe enough to bring her to the hospital.

Physical Examination.—The physical examination showed a pale, poorly nourished, white girl of normal intelligence. The head was symmetrical, and measured 48.5 cm. The pupils were equal and reacted to light. The ears, and ear drums were normal. The throat was normal. The heart dulness to per-

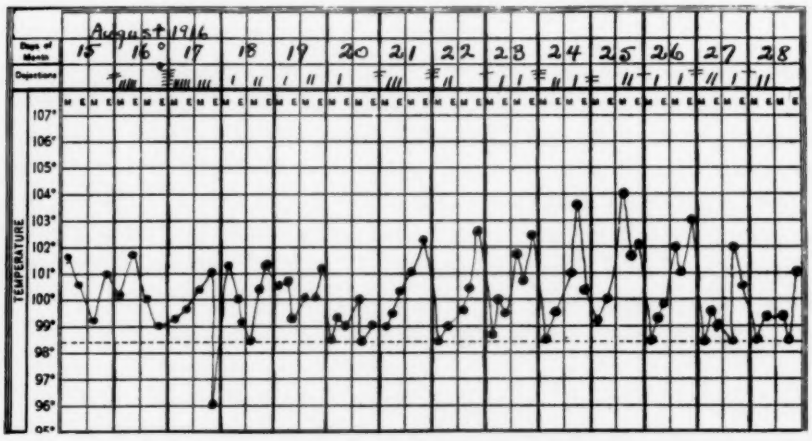

Fig. 1.—Sample of characteristic temperature for a period of two weeks.

cussion extended 2 cm. to the right and 6 cm. to the left of the midsternum. There was a slight systolic murmur over the precordia; the sounds were otherwise normal. The lungs were normal. The abdomen was very large, and when the child was prone, extended above the level of the thorax. The liver edge was palpable 4.5 cm. below the edge of the ribs in the nipple line. The spleen was very large, the tip being 4.5 cm. below and 3 cm. to the right of the umbilicus. The notch was easily felt. There were several patches of leukoderma, the size of a dime, on the chest. The reflexes were normal, and there was no enlargement of the peripheral lymph nodes.

The blood picture, shown in the accompanying table, with a low platelet count, 121, 324, led us to believe that we were dealing with an aplastic splenic anemia. The urine was normal on all examinations, except that now and then it contained the slightest possible trace of albumin, and a few red blood corpuscles. The temperature chart was found, later, to be characteristic in its irregularity. The accompanying four-hourly chart (Fig. 1) is a sample of two weeks which were typical of the course, during several months.

* Submitted for publication June 4, 1918.

BLOOD EXAMINATIONS DURING THE COURSE OF THE DISEASE

Date	Hemoglobin	Red Count	White Count	Differential Count					Remarks
				Small Lymphocytes, per Cent.	Large Mononuclears, per Cent.	Polymorphonuclears, per Cent.	Transitionals, per Cent.	Eosinophils, per Cent.	
8/15/16	32 Dare	2,460,000	3,000	41	38	15	6	...	Reds slight achromia; very little variation in size; no malaria; no parasites or blasts
8/18/16	45 Sahli	2,240,000	2,800	52	28	15	5		
8/23/16	29 Dare	1,800,000	2,600	61	22	15	2		
8/31/16	29 Dare	2,000,000	1,600	61	22	15	2		
9/ 3/16	23 Dare	1,696,000	1,600	17	80	3			
9/10/16	30 Dare	1,676,000	1,500	61	24	15			
9/20/16	25 Dare	1,960,000	1,600	42	37	20	1		
9/27/16	10 Dare	1,700,000	1,600	13	81	6	..	...	Two nucleated reds to 100 whites
9/29/16	.....	.....	.....	..	..	..	..	...	Transfusion
10/ 1/16	50 Dare	2,460,000	4,600	16	76	6	..	...	Slight variation in size and shape; no blasts or Jolly bodies
10/ 3/16	50 Dare	2,800,000	4,800	34.5	34.5	25	5	...	
10/ 5/16	40 Dare	3,000,000	4,800	19	59	16	4	4	
10/ 6/16	.....	.....	.....	..	..	..	..	...	Splenectomy
10/ 7/16	.....	3,520,000	.....	18	14	66	2	...	Twenty-three normoblasts, seven megaloblasts, to 100 whites
10/ 8/16	70 Dare	.....	5,000						
10/ 9/16	65 Dare	.....	4,800	14	5	81			
10/12/16	.....	.....	7,500						
10/17/16	65 Dare	3,456,000	6,600						
10/21/16	.....	2,912,000	6,800	..	..	..	..	...	One nucleated red
11/21/16	70 Dare	4,250,000	15,000	51	13	28	8	...	No nucleated reds
11/29/16	.....	4,260,000	17,000	42	2	54	2		
12/15/16	70 Dare	4,500,000	18,000	47	2	51			
12/24/16	65 Dare	3,840,000	13,000	38	27	33	2		Six nucleated reds per 100 whites
1/ 1/17	70 Dare	3,968,000	12,500	30	20	43	7		
1/ 9/17	65 Dare	3,408,000	15,000	17	20	59	4	...	Number of normoblasts and stipple cells
1/23/17	60 Dare	3,288,000	14,400	31	7	55	7		
2/ 5/17	75 Dare	3,976,000	18,000	33	8	54	5	...	Achromia; polychromatophilia
2/13/17	75 Dare	4,432,000	20,600	35	3	54	4	...	Some normoblasts; ++ platelets
2/23/17	75 Dare	3,864,000	18,400	22	7	57	4	8	
3/ 8/17	75 Dare	4,240,000	?1,000	46	4	45	2	3	No nucleated reds, ++ platelets
3/28/17	75 Dare	.....	20,000	71	1	25	..	3	No nucleated reds; platelets normal
3/16/18	95 Talq.	6,640,000	17,400	15	63	21	..	1	

Operation and Course.—Despite all treatment, the child lost weight and strength. Citrate of iron given subcutaneously was without any benefit. It was then decided to remove the spleen, but, because of the anemia, the operation was preceded by transfusion. Sept. 30, 1916, 200 c.c. of blood were introduced into the patient's anterior jugular vein by the indirect method (donor's blood, Group IV, patient's blood, Group IV).

October 6, splenectomy was performed by Dr. Beth Vincent, and a spleen, weighing 330 gm. was removed. The average weight of the spleen at 4 years is 42 gm.[1] The convalescence from the operation was without incident (Fig. 2).

Fig. 2.—Photograph of authors' patient taken Feb. 5, 1917, four months after splenectomy.

Examination of Spleen.—The spleen on section was firm, of a reddish color, and showed small, whitish areas scattered throughout. A striking feature of the hematoxylin stained section was a large endothelial phagocyte cell filled with dark blue staining spherical figures of fairly uniform appearance (Fig. 3, colored plate). There were large numbers of these cells scattered throughout the splenic pulp. Smear from the spleen, stained with Wright's blood stain, showed bodies about the size of blood platelets. These bodies had a sharply

1. Gundobin: Die besonderheiten des Kindesalter, Berlin, 1912, p. 172, Table 36.

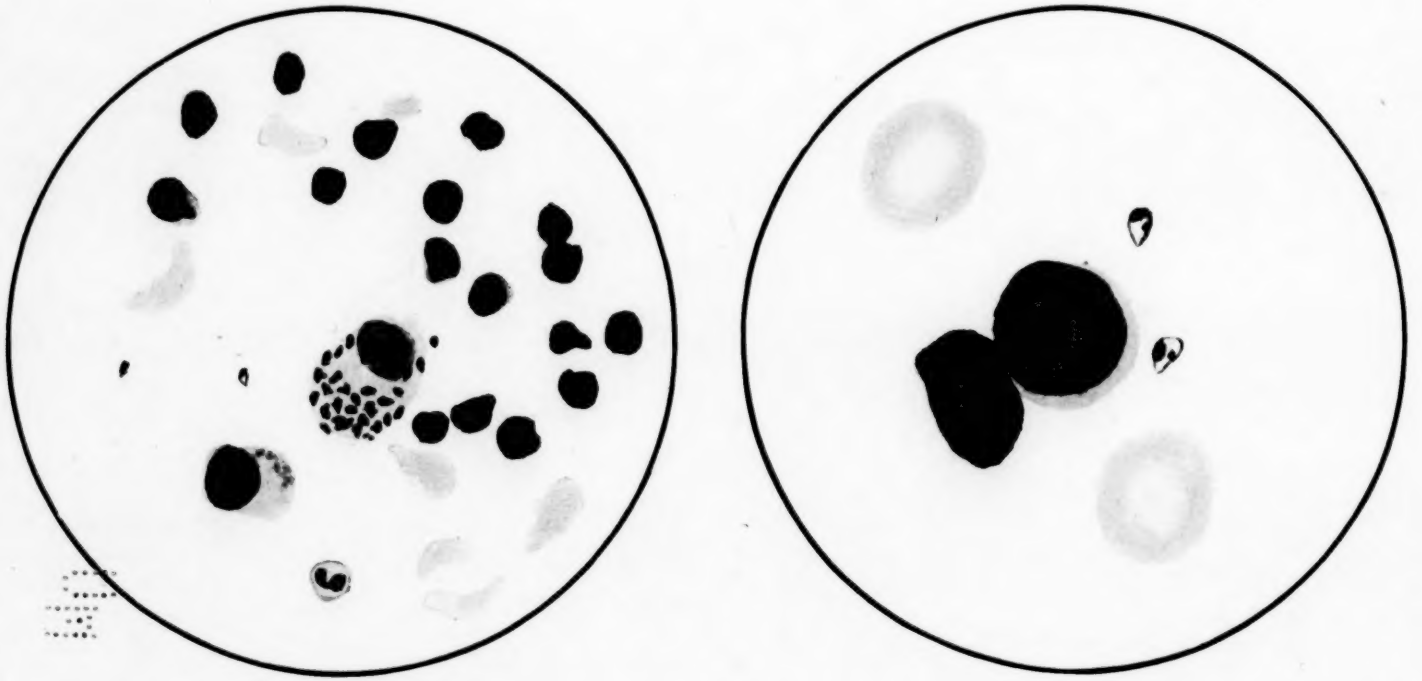

Fig. 3.—Kala-azar. I. Actual field. Smear from fresh spleen showing many of the Leishman-Donovan bodies enclosed in a large endothelial phagocyte. (Wright's stain.) II. Morphology. Single Leishman-Donovan bodies compared in size with lymphocytes and red corpuscles. (Wright's stain.)

Illustrating article of Fritz B. Talbot, M.D., and Arthur B. Lyon, M.D.,
American Journal of Diseases of Children, September, 1918.

outlined, blue-staining periphery, and an unstaining central portion, which contained two purplish staining structures. One of these structures was generally oval, sharply outlined, and occupied a part of the periphery. The other structure was smaller, more intensely stained, and had a red shape. These bodies were identical, in microscopic appearance, with *Leishmania infantum.*

Following the removal of the spleen, the child was noticeably better; she gained in weight and color, and was much more contented and happy. A blood culture at this time (October 31) was negative. A small inguinal gland was removed for diagnosis, and from it Dr. A W. Sellards was able to cultivate high, motile, flagellated organisms in large numbers (Fig. 4).

Subsequent Treatment and Outcome.—Intramuscular injections of atoxyl were given, beginning November 2, for one month, without any apparent effect on the course of the disease. She subsequently commenced to lose weight and strength rapidly and continued to run an irregular, intermittent temperature. The liver continued enlarged.

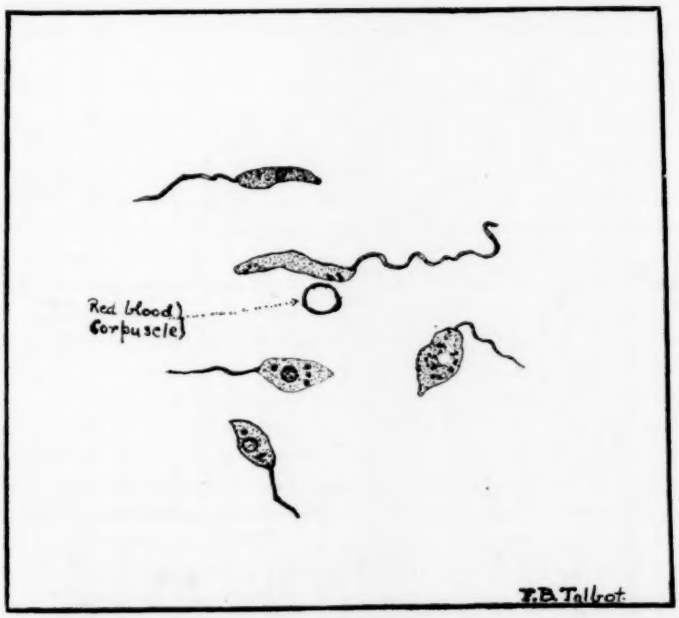

Fig. 4.—Culture of Leishman-Donovan bodies from inguinal gland of patient, K. K.

Following the suggestion of Sir Leonard Rogers,[2] a course of intravenous tartar emetic was commenced December 8. At first 1 c.c. of a 2 per cent. (0.02 gm.) solution was given daily, and later every other day, in increasing amounts up to 0.08 gm. When the tartar emetic was commenced the daily temperature varied between 99 and 104 F. One month later it had gradually subsided, and remained normal, with the exception of four days, until the child was discharged from the hospital. At one stage of its administration she was bothered by a cough, salivation, and loss of appetite, was irritable and cross, and remained in bed all day. The tarter emetic was, therefore, omitted; the appetite commenced to improve and the other symptoms cleared

2. Rogers: Lancet, London, Nov. 4, 1916.

up. In the meantime an abscess had developed at the site of one of the tartar emetic injections, causing the child considerable discomfort. After this was drained there was a marked and continuous improvement in general health and weight; she started to play around the ward and the size of the liver diminished, so that, on discharge, it could only be felt 2 cm. below the edge of the ribs. The child was discharged from the hospital apparently cured, March 28, 1917.

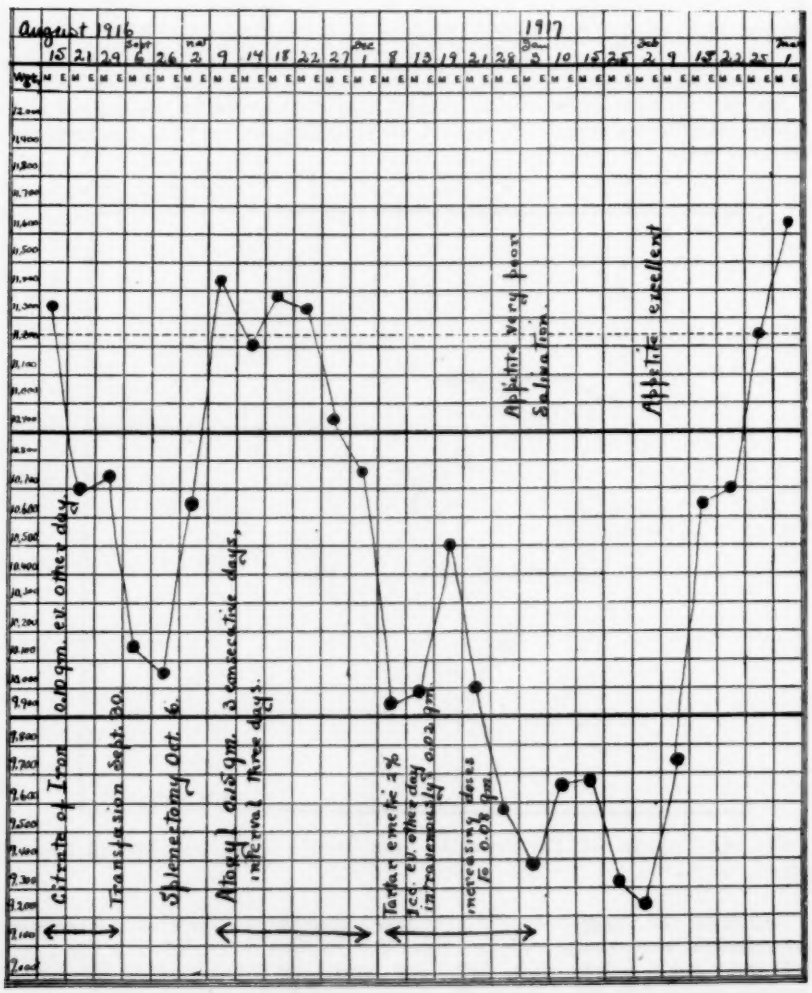
August 1916
1917
Citrate of Iron 0.09 gm. ev. other day
Translusion Sept. 30.
Splenectomy Oct. 6.
Atoxyl 0.15 gm. 3 consecutive days, interval three days.
Tartar emetic 2% sol. ev. other day intravenously 0.02 gm. increasing doses to 0.08 gm.
Appetite very poor Saline Iron.
Appetite excellent

Fig. 5.—Weight chart, showing operations and medication.

The accompanying weight chart (Fig. 5) shows the operation and medication during the period the child was in the hospital.

The child was seen in March, 1918, after having been home for one year. During the interval she was perfectly well, with the exception of having had diphtheria. Her physical examination showed that she was now well developed and nourished, with no enlargement of the peripheral lymph nodes, except a

very small gland in one groin, the size of a Number 8 shot. The heart, lungs and abdomen were normal. There were no masses felt. The liver edge was palpable just under the edge of the ribs. Her height was 94 cm., and she weighed 34½ pounds. So far as could be determined, she was an absolutely normal, healthy, well child (Fig. 6).

Fig. 6.—Photograph of child taken March 18, 1918, after having been home for one year.

DISCUSSION

So far as the authors know, this is the first case of infantile kala-azar reported in America. The disease is common in India, Asia Minor, and along the shores of the Mediterranean Sea. A few cases have been imported to England from these countries.

The parasites which bear the name of the Leishman-Donovan bodies were discovered by these investigators in 1903. They are also

found in dogs, and it seems probable that fleas transmit the disease from dogs to man.

The incubation period is variable. It may be as short as ten days or as long as several months.

The onset of the disease is usually insidious, but it may commence with chills and high fever. The fever is intermittent or remittent, the temperature chart often showing two remissions in twenty-four hours. The fever tends to last six weeks or longer and then declines. During the period of pyrexia the spleen and liver become enlarged, and through the course of the disease there is progressive loss of weight and increased anemia.

The duration of the disease varies, death usually occurring within a year from weakness or some complication. The prognosis is, therefore, bad.

Treatment up to date has been unsatisfactory. Tartar emetic 2 per cent. solution, may be given intravenously, as recommended by Rogers. It is impossible to say whether K. K. was cured by the tartar emetic or not, but the permanent improvement seemed to result from its administration. Further observations confirming these findings, and those of Rogers,[3] must be made before it can be accepted to be of proved value. Improvement from splenectomy is, as a rule, only temporary. Other methods of treatment are without value.

311 Beacon Street.

3. Rogers: India Med. Gaz., 1917, **52,** July and August.

CURE OF A SYPHILITIC MENINGITIS BY ARSPHENAMIN AND MERCURY

SYMPTOMS—CONVULSIONS AND INTENSE OPTIC NEURITIS—DEVELOPED AFTER A HEAD INJURY *

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The writer presents the history of a case of luetic meningitis in a child. The condition, although not unusual, has received scant attention in pediatric literature.

REPORT OF CASE

History.—The child was well up to March 1, 1917, when he fell from the roof of a standing freight car, striking on his head. After the accident he seemed in great pain for several hours. During the night he had a chill and vomited until morning.

Two weeks later he commenced to have crying attacks and twitching and pain in the left arm.

These emotional attacks increased in severity and were associated with convulsions, which occurred every second night.

Four months after the injury (July 10) the patient entered the Buffalo General Hospital as a case of epilepsy. During the first ten days of his stay he had one convulsion, frequent screaming attacks and periods of maniacal excitement. He cried, swore and talked incoherently, and complained of pain and muscular twitching in his left arm. After a few days it was noticed that his movements were awkward and constrained; that he held his head and back very rigidly, the head being inclined to the right.

Examination, July 20.—He was a well developed boy of 10 years. The neck was very stiff and difficult to bend backward; no tenderness of the skull or neck; spine normal in contour but restricted in motion and very rigid; tenderness and muscle spasm along the vertebrae and in the right flank. A roentgenogram showed the cervical and dorsal spine to be free from disease The knee jerks were very active; ankle clonus of right leg; Kernig sign present, most marked on right side; muscles of arms and legs very spastic. The pupils were widely dilated; reacted to accommodation but not to light. There was a double optic neuritis of 2 diopters, each side. Leukocytes, 9,350; hemoglobin, 80 to 90 per cent.

By lumbar puncture 10 c.c. of fluid were obtained under moderate pressure: it was colorless, turbid and contained 466 cells per cubic millimeter. Globulin and albumin were each ++++; Wassermann, ++++. The father and mother each showed a Wassermann ++.

Diagnosis and Treatment.—The child was evidently suffering from a syphilitic cerebrospinal meningitis. He was given daily inunctions of mercury and arsphenamin every one or two weeks.

After the first dose of arsphenamin there was a prolonged chill and fever of 102 F., the only rise of temperature in the disease.

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* Submitted for publication June 12, 1918.

*Read at the Annual Meeting of the American Pediatric Societay, Lenox, Mass., May, 1918.

Course.—August 5. There were several screaming attacks and one long convulsion.

August 6. Swelling of the optic disks was much increased; most marked on the right side. The child said he could not see. There were severe root pains in left leg, right hip and shoulder.

August 10 to 26. During the next two weeks the child grew steadily worse. The screaming attacks and convulsions were very frequent. One day the child had four convulsions. He complained continually of root pain in his arms, legs and back. His mental condition was much disturbed. The child scarcely spoke at all; was slow of comprehension, disobedient, hard to control, executed simple orders slowly and with difficulty; often struck the other children in the ward.

The neck and back were very stiff. It was almost impossible to elicit lateral and backward movement.

Choking of the disk was very marked; right 4 D.; left 3 D., indicating increased intracranial pressure.

Spinal puncture gave 25 c.c. of fluid under pressure; very cloudy. Globulin and albumin were ++++. The cell count was 1,700 (contrast with five weeks before: cell count 466), showing an increase in the meningitis.

August 27. No convulsions; severe root pains in the arm. The oculist stated that the optic neuritis was increasing and gave a bad prognosis as to vision.

September 3 to 6. There had been crying attacks and convulsions. Note that in the previous two weeks the convulsions almost ceased, but a steady increase in intracranial pressure was shown by the condition of the optic disks.

Two lumbar punctures gave no relief, and September 8, the oculist gave a last urgent warning that the swelling in each disk was 6 D., indicating dangerous intracranial pressure, and that blinding was imminent unless a decompression was made.

September 8. Decompression and aspiration of the right ventricle; 50 c.c. of fluid withdrawn. During the next ten days the child vomited frequently, was restless and screamed a great deal; no convulsions. The swelling of the optic disks subsided to 4 D., then increased to 6 or 7 D.

September 21. The right ventricle was aspirated; 15 c.c. of phenolsulphonephthalein solution were injected into the ventricle. Two hours afterward phenolsulphonephthalein was found in urine; two and a half hours afterward no phenolsulphonephthalein found in spinal fluid.

After the aspiration the boy was very restless for forty-eight hours and had a long convulsion, relieved by chloral. The optic disks were daily examined, but the aspiration produced absolutely no improvement. After two weeks a slow reduction in the swelling occurred. A month later the swelling amounted to 2 D.

There were no convulsions or mental disturbance after September 24.

October 22. The boy was in very good condition; ate and slept well; was active about the wards and out of doors. The mental dulness had disappeared; understood and obeyed quickly; was able to draw squares and circles, write name and address; was very responsive when given Swedish gymnastics; was mischievous and had to be frequently reproved.

Sensation was everywhere normal; head held to right; slight limitation of movements of head and spine; no local tenderness, neck, skull or back; mouth habitually open; pupils dilated; Kernig's sign present; knee jerk active; no ankle clonus.

Spinal fluid clear; 13 lymphocytes per cubic millimeter. Wassermann and colloidal gold test positive. Wassermann ++++ to 6 c.c.; negative to 0.4 c.c. Lange colloidal gold test = luetic curve, 1.5, 1.5, 2, 1.5, 1.5, 1, 1, 0, 0.

During November and December there was continuous improvement. About December 24, the Wassermann was negative, and the optic neuritis had dis-

appeared. The boy was sent home and attended school regularly. In April he complained of frequent momentary headache. The spinal fluid, however, was negative to the Wassermann and colloidal gold tests. About May 1, the optic disks were normal.

On May 14, fourteen months after the beginning of symptoms, the child was free from all symptoms and had been for seven months.

INTERESTING FEATURES OF THE CASE

1. Neither the parents nor the child had any symptoms of syphilis, hereditary or acquired.

2. The fall on the head acted as a provocative agent causing cerebrospinal symptoms in a case of presumably latent hereditary syphilis. This, of course, is not unusual. Nonne believes that the importance of head injuries as a cause of cerebral syphilis is overestimated, and also says that these accidents do not cause especially severe forms of luetic meningitis; extensive affections of the interior of the brain may remain entirely symptomless. In the development of the brain symptoms of syphilis, nervous heredity or neuropathic constitution has absolutely no influence.

3. The lesion in the cerebrospinal meninges was probably a proliferative gummous leptomeningitis involving the cortex and spinal meninges; also in ependymitis with an increase of cerebrospinal fluid and some hydrocephalus. The choked disks were due to intracranial pressure from fluid and not to a direct inflammation of the optic nerve.

Optic neuritis is present in 40 per cent. of cases of cerebral syphilis. Ophthalmologists tell us that a high grade choked disk is usually a simple edematous saturation and may exist without disturbance of vision or injury to the retina, subsiding under antisyphilitic treatment. If the process is allowed to progress it may cause partial optic atrophy. In this case the course, increase and gravity of the brain symptoms was discovered and controlled by the oculist, Dr. H. W. Cowper. Every case of supposed epilepsy should have the fundus and spinal fluid examined.

Heubner emphasizes the frequency of epileptic convulsions in syphilis; of forty-five cases of gummous meningitis twenty-five patients had convulsions. Contrast the absence of fever with the fluctuating temperature of tuberculous and other meningitides.

4. The decompression and aspiration were followed by no immediate relief save that the lessening of intracranial pressure gave the cerebral circulation a little more freedom.

The patient was very responsive to treatment; the acute symptoms lasted about three months. Mercurial inunctions were given every day for five months and arsphenamin at first every week; later every two weeks.

The cure of syphilitic meningitis even before the days of arsphenamin was not infrequent. Of Nonne's cases of cerebral syphilis only two were between the ages of 1 and 10 and one between 10 and 20. All improved.

The same author using only mercury and iodid reports 71 per cent. of recoveries, acquired and hereditary syphilis having the same prognosis.

In syphilitic meningitis of the convexity, with partial and general epilepsy and alarming and characteristic symptoms, recovery is common. Relief is more certain if specific treatment is used early. Oppenheim and Ehrlich have the impression that in the present era of arsphenamin, cerebral symptoms are more frequent, owing to slight nerve injury rendering the tissue more susceptible to the irritation of syphilis. Oppenheim questions whether the Wassermann test of the blood and spinal fluid is a criterion for the continuance and repetition of therapy. The writer received much assistance in the management and treatment of the case from Dr. H. W. Cowper and Dr. E. H. Sharp.

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PSYCHOGENIC DISTURBANCES IN CHILDHOOD AND THEIR TREATMENT*

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Psychogenic diseases play an important rôle in childhood; they are at this period of life much more frequent and their nature is more easily demonstrated than in the adult; they are to a high degree subject to the influence of suggestion therapy and therefore possessed of a paramount importance in the practice of the pediatrician. The necessity of the recognition and appropriate valuation of the psychic elements in the complex of clinical syndromes cannot be emphasized enough.

DEFINITION

We understand by psychogenic diseases those disorders that emanate and originate from psychic processes, namely, from conscious, subconscious or unconscious ideas, associations, conclusions and impressions with or without accompanying emotions of the affected child. Though many of such disturbances are of hysterical nature, we must be cautious not to identify hysteria with the much broader term of psychogeny. Pain, fear, anxiety and worry, for instance, accompany in the adult perhaps every important somatic disease and lend a peculiar color to the clinical picture; their effects are closely interwoven with the purely organic symptoms through mutual interaction.

In the human mind there is a continuous current of mental processes, of associations, thoughts, ideas and conclusions and emotions, which to a great extent are underneath the surface of the clear consciousness, but which nevertheless leave residual imprints on the central nervous system, not always merely temporarily, but also of some duration and permanence in the form of subconscious or submerged memories and "facilitations." It was the merit of Freud and his school by his analytic methods to have brought the obscure, often deeply buried psychic elements and their intricate relation to somatic disturbances of neurotic character into the compass of scientific research and put them into a clearer perspective and better appreciation by the profession.

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The psychogenic disturbances that are the subject of discussion in this paper may manifest themselves in the sphere of almost any organ, and the aspects of the symptoms are numerous and various. There is scarcely an organ that may not display nervous disorders of the nature of psychogenic reflex processes. They embrace the sensory, secretory and voluntary motor functions as well as those of the smooth muscles that are not directly subject to the will, as those of the gastro-intestinal tract and of the heart.

The psychomechanism, the methods of operation of the provocative occasions and agencies, and the sources of the disorders are of various nature. The latter may be due to imitation and psychic contagion, that is, have their cause in the "suggestion" or reflex receptibility which is a cardinal attribute of psychic life.

The special proneness of children to imitation, their great susceptibility to impressions, their impressionability on account of the immaturity, instability and undevelopment of character, the credulity, vivid imagination, belief in authorities and lack of logical criticism convert example, in their case, into a mighty, almost magic force, both in the psycho-physiologic as well as the pathologic direction.

IMPORTANCE OF EXAMPLE

In the presence of these peculiarities of the psychic life and on account of its tendency to discharge physical reactions on impressions, the environment or milieu of the child is possessed of momentous import. Therefore, no wonder that a disease, observed in another person, may be mirrored in the psyche and give rise to similar morbid symptoms in children. Particularly will a neurotic, hysterical person render others in contact with him, likewise nervous in the course of time, and the latter will often acquire and appropriate, as it were, certain nervous disorders and habits.

The danger of forming and stabilizing such nervous disorders, induced by the imitativeness and suggestion is, of course, with the child greater than with the adult.

We also frequently make the observation, that children affected with minor ailments will in different environments and surrounded by different persons present great variations in the clinical picture aside from the uniformity of the otherwise, of course, identical diseases, and act differently. Factors not lying within the nature of the pathologic processes themselves, but those of entirely extraneous characters, namely, the influences of the change of milieu, will call forth a change of the symptom complex in its nonobligatory, not organically caused, features; the impressionable plastic psyche of the

child being affected by the transformative circumstances as clay or wax is shaped under the hand of the modeling artist.

The great historical examples of prodigious psychic epidemics, such as the children's migrations and crusades, the dancing manias, great choreas (St. Vitus' dance), etc., demonstrated the sweeping extent and overwhelming intensity of the suggestion, the power of example and the force of a "contagion idea" as Hecker, a physician, has depicted it with the pen of a historically and psychologically well trained writer.

Also the well known psychic school epidemics of our times, that are recorded in medical literature, give testimony to the great forces dormant in the human mind. For example, we cite the epidemiclike occurrences among many school children of the same classes of tremor, singultus, choreatic movements, disturbances of handwriting, enuresis nocturna, sleeplike states and other peculiar phenomena of the so-called imitation or induction diseases.

For the individual physician more important are the sporadic, isolated cases of psychogenic disturbances of imitative origin. They represent a great variety, they are protean and may affect the nervous system, the psychic sphere and the vegetative functions. As I have dwelt on this feature in a former essay, I may here only summarize, that in children in very numerous instances motor, sensory and visceral disturbances, such as for instance, attacks of limping, tremor of paralysis agitans with more or less exactness of the crude clinical picture, facial and other *tics convulsifs,* peculiar dyspneas or types of respiration, backache or pain in the chest, in the limbs, in the side or the abdomen, heart palpitations, vomiting, etc., could be traced to no other etiologic factor than to the suggestive influence of the example of their parents, most often the mother, who would complain day by day of their own ailments and pains, imaginary or real, in the presence of their children. The nervous parents through their conduct awake in the child corresponding ideas and impressions and guide its imagination in a certain pathologic direction. Such parents also by their anomalies of character in the sphere of emotion and volition are bound to be of immense educational detriment to their children, aggravating the effect of an hereditary neuropathic constitution by the influence of a morbid environment, the neuropathic milieu.

AUTOSUGGESTION

But perhaps more than the ailments of others do the child's own diseases influence its psyche. The subjective symptoms of an originally organic disease, as a rule painful or involving the motor function, will be aggravated or prolonged psychogenically. For instance, after

a catarrhal laryngitis hysterical aphonia may follow; or after tonsillitis, that had kept the patient bedridden, abasia and astasia; or blepharoclonus may remain after the subsidence of acute conjunctivitis or the removal of a foreign body.

Pain, after the complete cure of its organic basis, will become fixed as psychalgia, as *douleur d'habitude* (Brissaud's), as habit pain; the latter will be, so to speak, the reverberation of the previously actual pain that accompanied some organic disease. Such disturbance represents a condition brought about by auto-imitation of the original disease; it is the psychogenic residue, "the declaration of permanence" (Bruns) of the subjective symptom of the previous organic disease.

After the disappearance of acute rheumatic polyarthritis, a psychogenic residual pain may persist for a long time and may even be of a very violent nature; these arthralgias may be so intense as to forbid the slightest touch while the child is aware of it, but will disappear entirely if the attention is diverted or in the sleep, so that the child will lie in any position on the affected part.

As classic an example as one could wish to demonstrate this condition is described in the following case:

O. A., a boy aged 5 years, had the following history: Three months ago he became ill with pains in various joints; the left knee particularly was swollen and reddened for awhile; it remained painful permanently. Two months later pains in the right knee, in the ankles and shoulder joints supervened. He had been three months bedridden, when he was admitted to the Cook County Hospital. The boy, when seen by me for the first time, manifested extreme pain on the slightest touch or attempt at passive movements of both hip and knee joints; they were contracted and held in moderate flexion. The feet were slightly painful to pressure. Swelling was not present anywhere. During sleep the contractures, however, disappeared and time and again the boy was found lying in any position of the affected limbs. There was also free passive mobility, if the child's attention was sufficiently diverted by various tricks. It was indeed a classic example of the psychogenic character of residual, though very vehement pain. After a few days the pain had disappeared completely, but the boy, while rather freely using his legs in bed where he liked to play cheerfully, was entirely unable to stand or walk, manifesting complete astasia and abasia. This astasia and abasia proved rather refractory, perhaps as a result of too much attention and interest shown to him in frequent clinical demonstrations. After about four weeks he rather unexpectedly was found standing up in his bed and climbing over the railing into his neighbor's with remarkable skill, but he was still unable to stand or walk on the floor. Then, for therapeutic reasons his legs were submerged in cold baths twice a day and within three days the control of his legs was restored.

Other patients manifest painful sensations or motor disturbances, as contractures and pseudoparalysis that persist obstinately subsequent to a perhaps insignificant trauma. Two instances that could be multiplied may suffice to exemplify the statement.

The 8-year-old son of an artist after a fall on his right shoulder during play suffered from vehement pain and stiffness of the joint for several days, when

on examination no lesion could be found. The roentgen-ray examination revealed no lesion. The free passive mobility of the joint when his attention was distracted, and the rather sudden disappearance of pain and contracture after a merely suggestive treatment proved clearly the psychogenic character of this residual disturbance.

M. S., a girl, aged 12, three months ago when playing, fell forward on the pebbly ground in front of the school. Two days later dull pain in abdomen and headache of a shooting character appeared and has persisted in the form of daily attacks since then. The abdominal pain appeared independent of the meals and the headache occurred every morning and evening, continuing for about one hour; they were brought on or aggravated especially by excitement. There were no objective signs of any injury, but painfulness of the lateral and lower parts of the abdomen on pressure was present. A verbal suggestion emphasizing a complete cure in conjunction with abdominal massage on the spot, brought about the immediate disappearance of the pressure pain. A few drops of tincture of valerian were ordered daily. The headaches and pains in the abdomen never returned.

To show what queer pranks autosuggestion may play on a child, the following case exhibiting a component of phobia may be here reported.

An intelligent boy aged 7 had short but frequent attacks of a feeling of constriction in his throat and inability "to swallow the saliva," causing him "fear of choking." A swallow of water would forthwith relieve the distressing symptom. These attacks by their frequency caused him so much anxiety, that finally he was afraid to go where he would not be able to get water if in need. When outdoors he chose streets or places where he would find a well or pump nearby. On one occasion a more severe attack seized him suddenly in a long street, so he had to hurry to a well; drinking gave immediate relief; but as soon as he had left the well, another attack compelled him to return forthwith; this happened several times in close succession; it was only with apprehensive hesitation, that he ultimately went home. The attacks continued over one week. The boy was otherwise perfectly healthy.

The only explanation I could find of this peculiar disturbance manifested in this boy was perhaps either the possibility of a previous tonsillitis or more likely in combination with the fact, that the boy's phantasy had been much aroused by stories about "choking and impossibility of swallowing" in a case of hydrophobia that had occurred in the town.

The auto-imitation of a previous organic disease, the fixation of a symptom in the psyche, indeed often is directly cultivated and fostered by the overanxiety, morbid solicitude, apprehension, overindulgence and imprudence of some parents. They may by asking the child over and over again after this or that symptom keep the latter alive in the mind of the sick child, or they may yield to every desire and wish, however foolish, of the sick child out of excessive sympathy, and multiply their manifestations of parental care, so that there seems to the child to accrue more advantage from being sick than from being healthy.

This fact holds also true of the so-called oneirogenic (dream-

produced) disturbances of sleep; as for instance, of somnambulism. As is well known, nervous, especially hysteric children, may occasionally leave their bed due to restless sleep, vivid dreams or fears. If the parents show themselves unconcerned, as a rule the attacks will rapidly disappear spontaneously. However, if much concern is shown and apprehension expressed in the presence of the child, in a number of instances rising from bed and sleep-walking will become more frequent and the morbid tendency aggravated. By ignoring the condition and removing the child from his obnoxious home environment, these procedures, as a rule, soon correct the sleep disturbance, proving by the influence of suggestion its psychogenic nature.

COMPLICATING FACTOR

Not only may the psychogenic factor assert itself in prolongation of pain after the subsidence of the organic cause, but — as passingly said before—it may also during the organic stage of a disease by aggravation exaggerate the clinical manifestations, or add to the organic complex another complicating symptom which may be recognized as neurotic by the prompt effect of psychic treatment, as will be discussed later in extenso.

The following case will exemplify such an element of psychogenic complication of rheumatic chorea minor.

M. S., a Jewish boy, when admitted to the Cook County Hospital, manifested the symptoms of chorea minor of moderate degree. This was the third recurrence within two years. Lately, according to the history of the case, attacks of violent tremor of both upper extremities had supervened; they continued as long as two hours without cessation, and occurred on some days several times, particularly starting under the influence of excitement and anger. This "trembling" consisted of very rapid pronatory and supinatory rotations of both forearms, the extremities being held spastically extended in the elbow joints, and directed downward. This "trembling" evidently not belonging to chorea minor, never appeared in the hospital and thereby documented its accessory character. The analysis of the etiology made it appear as very probable that the tremor had developed originally from the ordinary tremor that accompanies the effect of anger and wrath.

It is probable that in childhood all psychogenic disturbances originate in some actuality, either in a real organic somatic disease, or in psychic traumas, especially in impressions and experiences that react through the reflex of imitation, or in physical traumas with psychic by-effects. It is not only the severe acute psychic traumatism, that as a provocative factor of neurotic disturbances comes into consideration, but often also the small, apparently insignificant, not dramatic psychic insults, that, if repeated, may have and do exert a cumulative effect. Thus, particularly in the school age, injustices on the part of teacher or schoolmates, disappointments of expectations, frustrated

ambitions, excessive aspirations overstimulated by the parents, anxieties, fear of examinations, etc., may act as slight but continuous injuries on the sensitive psyche especially of predisposed, angiasthenic, vasoneurotic and impressionable individuals. They may give rise to various morbid manifestations as, for example, heart palpitations, precordial pain, vertigo, etc. Exciting scenes of an unhappy home life act in the same way.

REFLEX INFLUENCES

Many phenomena explained as due to auto-imitation and classified among the manifestations of monosymptomatic hysteria have to be considered as nothing else but "pathologic conditional reflexes," the definition of which Ibrahim has circumscribed, introducing it into our clinical terminology, in his exposé, following Pawlow's doctrine.

A typical example, representative of the conditional reflex of pathologic character is illustrated by the so-called pertussis tic, the *"tic coqueluchoide"* of Lesage and Collin. As generally known, especially neurotic children, suffering from whooping cough, will for an unduly long period, even for months, continue to have attacks of spasmodic cough; this with the exception of its nonproductiveness of sputum, will mimic the typical pertussis. The children, in a number of instances, may call forth these attacks voluntarily, in order to impress their anxious, apprehensive environment and enforce their capricious will. In other instances, the cough due to acute bronchitis or pharyngitis, if acquired weeks or months after pertussis, may likewise copy its type. Striking therapeutic results are to be obtained at this stage within a few days or even at once by the application of methods that act merely through suggestion and are so successfully employed in hysteria of childhood, as by intentional neglect, brusque commands, energetic orders to suppress the cough, if necessary with emphatic threat of punishment or other educational means. This fact characterizes the nature of the disturbance as an acquired "pathologic conditional reflex" (Ibrahim). The cough impulse constitutes the stimulus for the conditional, semi-voluntary reflex. The children need only produce a few cough impulses either purposely or impelled by broncho-catarrhal or pharyngeal irritation, in order to have started the entire mechanism. The rapid cessation of the attacks, once the child has succeeded in suppressing them a few times under the influence of therapy or by avoidance of their provocations, indeed is in keeping with the extinction of a conditional reflex in the animal experiments of Pawlow and his pupils, or in the experiments of Krasnogorski in children. The fundamental investigations and achievements of these authors, indeed, have thrown a bridge into a new field of fruitful and promising scientific research.

The conception of an acquired pathologic conditional reflex finds its ready application in "respiratory affect-convulsions," or rage spasm, the apnea in anger-paroxysms (Wegbleiben) of neurotic children. By suddenly springing a surprise, by diversion of the child's attention, by threats or a slight slap, such psychogenic paroxysms can be suppressed in the very start, as a conditional reflex in the animal experiment will be inhibited by the introduction of a new stimulus.

Also the not infrequent nervous vomiting of children in the morning before or on the way to school, may be traced to a psychogenic origin, perhaps under the cooperative, auxiliary influence of emotions, the psychic reflex act of vomiting being firmly anchored to the idea of going to school. In educating babies to defecate or urinate at a given regular time by bringing them on the chamber, we intentionally create a normal conditional reflex, the automatic act of defecation or urination becoming psychically anchored to this newly introduced stimulus. In many adults various sensory impressions, as, for instance, hearing water run, will facilitate the act of micturition, this acoustic stimulus, once established, serving here as an acquired conditional reflex stimulus.

In a boy, aged 5 years, for one and one-half years free bowel movements were obtained only every other day by a small enema; without the latter he obstinately refused to defecate. For him the enema evidently represented an acquired but apparently indispensable psychic stimulus more than anything else. The enemas for therapeutic reasons were completely discontinued, and after a few days of constipation the boy became convinced of his ability of spontaneous defecation, thus acquiring the normal habit.

The following neurotic disturbance, observed by me lately in the dispensary of the Rush Medical College may be cited.

A boy, aged 9 years, fond of school work, has suffered for several years from abdominal pain, that continues regularly from about 10 to 12 noon and from 2 to about 3:15 p. m. A close examination revealed, in addition to a slight diastasis of the recti muscles, rigidity of the abdominal walls and pain over the entire abdomen on pressure. The fact that the pain never appeared on Saturdays and Sundays or during the school vacations revealed the merely neurotic character of the disutrbance; its rapid improvement after a single application of the faradic current, and its complete disappearance within two weeks confirmed the diagnosis. The boy received a few drops of tincture of valerian daily.

ONEIROGENIC DISTURBANCES AND PAIN HALLUCINATIONS

It is a not sufficiently noted but very noteworthy fact, that also oneirogenic disturbances, that is, those due to the operation of dream-ideas or dreamlike states are amenable to the salutary influence of suggestive treatment, applied during the waking state. Not only pavor

nocturnus, somnambulism and allied anomalies fall in this class, but also disturbances as illustrated in the following observation.

B. H., a girl, aged 11, suffering from headaches, awakes suddenly from her sleep between 10 and 12 p. m. with violent pains in the region of the stomach, but immediately after falls soundly asleep again. Sometimes this attack may occur in the same night a second time, rarely a third time. The attacks return at rather regular intervals of a fortnight during the past six months. For the past two days she also suffers from pains in the rectum, spontaneous and independent of defecation. Her brother suffers from enuresis nocturna. Inspection and digital examination of the rectum revealed no anomaly, but complete relief of pain resulted immediately. The definite disappearance of the nocturnal attacks of gastralgia and vomiting, for which no organic cause could be detected, on a mere suggestive medication (a few drops of syrup of ipecac) and verbal assurance of cure brings forth into clear view the psychogenic element of this disorder.

Oppenheim has called attention to the relation between certain pains, the so-called hypnalgias and the processes of sleep. A number of his adult patients had suffered from cardialgias or neuralgias that aroused them sooner or later after falling asleep and persisted only a short time after awakening, appearing again as soon as they yielded to the desire to sleep. These pains never began in the waking state. Whatever the explanation may be, in a number of his cases the origin of the disturbance has been, in the view of Oppenheim, probably due to pain hallucinations, that like other sensory illusions are in connection with dreams.

If attacks of fear, ringing in the ears, of pain or paresthesia exacerbate during the night, it may also be due to the patient giving them more attention to his somatic processes or because of the abrogation of the influences of the higher nerve centers.

Hamburger has turned his special attention to sleep disturbances in children, repeatedly observed also by Popper, of an oneirogenic origin, as whining, moaning and complaining, almost exclusively in the sleep, as abdominal pain, or vomiting or coughing attacks without awakening, that yielded readily to simple suggestive therapy (psychotherapy).

Such observations seem strongly to oppose the presumption, no more to be maintained, that pain, cough or vomiting, because occurring during sleep, must necessarily have an organic origin in every instance. Indeed, the sometimes striking curative effect of psychotherapeutic methods, as change of milieu, pedagogical influences, etc., in enuresis nocturna has long been an argument additional to those that likewise proved the correctness of the assumption of its inorganic origin.

TREATMENT

The psychogenic disturbances, with certain very obstinate exceptions, as a rule are very readily curable through various means that are essentially psychical. In psychotherapy we attempt to exert our

influence on the idea, idea-complexes, sensations and emotions of the child; and thereby to act on the functions of the various organs through their close relationship to the psyche. It is superfluous to emphasize the necessity of an exact physical examination, so as not to overlook a somatic disease.

Disturbances of an imitative or induction origin will urgently necessitate the elimination of the inducing person or the removal of the child from his former obnoxious environment; otherwise, when this is impossible, one must not be surprised by recurrences. Yet, even then, permanent disappearance of the symptom in a number of instances were obtained, if the parents carried out the instruction not to make an exhibit of their own affections and by permanent complaining and mention of their own ailments to accentuate the baneful influence on the impressionable child. Czerny proposed for children suffering from pertussis, not to be kept in the same room, since the paroxysm in the one patient will often provoke an attack in the other.

In many cases, the intentional neglect of the child's morbid manifestations will have its important place; especially in irritative conditions, or when previously too great solicitude on the part of the environment, fostered and nurtured as mentioned before, the psychic fixation of the ailment and kept it permanently alive in the mind of the patient. The child may be directly told that his trouble is a minor one, that he exaggerates, or no word may be dropped in his presence, the ailment apparently disregarded and the child observed only without his knowledge. Many a symptom will thus be suppressed in the start. Cessation of the psychogenic complex will spontaneously ensue within a short time, once the child finds no more his sympathetic and interested "public." "The symptoms will gradually die of ennui. The child forgets them, so to speak, altogether" (Bruns).

A pathologic psychic reflex, occurring habitually, may be abolished either by not allowing the provoking "memories" to appear or by linking them up with new displacing associations; thus the unfolding of the former habitual associations—those in the waking state as well as those occurring during sleep—will be frustrated and entirely dislodged. Such memories are especially likely to fail to appear or to be entirely dislodged, if the child's entire life is radically altered, namely, by a complete change of its environment, as for instance by separation from the accustomed surroundings, the removal from the paternal home to a hospital. In other cases the change of the personnel, the introduction of a new attendant or sober-minded nurse will suffice to dislodge the morbid complex.

It is true, an alteration of the milieu in outspoken, hysterical children must be radical and comprise not only a change of place, but in

addition, also the absence of visitors, especially the separation from family members, the leaving at home of toys and books or other objects that have been in frequent use by the child and therefore are closely connected and interwoven with his manifold associations and morbid complexes of ideas and emotions.

These facts give us the explanation, why we encounter so rarely in hospital practice disorders like somnambulism, pavor nocturnus and other allied oneirogenic disturbances, for evidently the children go to bed with entirely different ideas and thoughts than before, and the previous habitual or stereotypical dream-ideas with their psychomotor reactions do not come into existence.

It is worth recalling to mind the interesting fact, as Friedjung has emphasized, that sleep disorders not of oneirogenic origin, as difficulty in falling asleep, interruption of sleep and wakefulness of children in the night, with restlessness, asking questions and fitful desires and other evil sleep habits may also in most instances be corrected by such simple means as change of the bedroom. A slight change in the arrangements of the life of the child immediately before bedtime will likewise have its effect.

It will often have a most salutary effect for the child to meet and play with healthy and vigorous children; this will more than anything else divert his attention from his physical condition and, indeed, the imitative instinct of the neuropath by being directed into other channels will thus be utilized in bringing the child back to normal habits and tendencies.

Effectual and powerful as the change of milieu may be, circumstances will not always render it expedient, feasible or necessary. We will have to resort to other methods, all aiming likewise at diverting the child from his disturbances and altering favorably his entire conceptions, ideas, deductions and imaginations, conscious as well as subconscious.

Psychotherapy will here have to be addressed directly to the child through simple verbal suggestions, particularly with the support of appropriate apparatuses, auxiliary manipulations, as massage, medication or other supplementary physical means, that impress themselves on the child's mind as wonderful, mysterious or novel, and mask the psychic element of the treatment. The influence of suggestion may reach even the sphere of oneirogenic phenomena and other sleep anomalies, as has been mentioned before.

The certainty, often the rapidity, of a cure may be surprising to the observer, as the mere authoritative word, the emphatic and positive assurance of cure, or, according to the individuality of the patient,

kind persuasion, encouragement and tact, reward or punishment, will remove the disturbance, the medicine administered serving merely — so to speak — as the "visible symbol and token of the invisible force." The authoritative, determined appearance of the physician, his "personality," the firm confidence of the little patient and his belief in the physician and his orders are the *conditio sine qua non* of a successful treatment of purely psychogenic ailments. Polypragmasy must be avoided. It is the How of administration more important than the What.

It would be preposterous and destructive of the physician's purpose, unwarrantedly to designate these "neurotic" disturbances as hysteria to the parents, who not infrequently resentfully would assail the physician's diagnostic acumen for this terminology, that is so utterly unpopular among laymen.

There is, of course, nothing novel in the principle of these methods, and psychotherapy has been practiced successfully from the beginning of empirical medicine, remaining throughout the ages inseparably connected with our art of healing. However, it was not only then that the disciples of the hippocratean art were unaware of the great therapeutic import of the psychic forces that their words, orders and prescriptions carried; that they scarcely suspected the paramount rôle psychic elements play in the composite aspect of the clinical pictures. They hardly could realize the true and real nature of the curative agency and principle. Wherever an adequate appreciation and appraisal of the psychic moments is still wanting, self-deception is likely to follow and without criticism to attribute too much merit to pharmaceutical preparations; this will lead to a regrettable neglect of a therapeutic principle that in systematic and rational application is bound to yield excellent results, far better than in the hand of the merely intuitive user among our profession, not to speak of the commercial faith healers, Christian scientists and other false prophets without any medical training, but with much pretension and arrogance.

I often found it good procedure to hold out and reiterate the prospect of cure not directly to the child, but in his presence to his mother, or in my dispensary work, in addressing the students, augmenting thereby the suggestive effect by the prestige and authoritativeness of the teacher.

By force of verbal suggestion, aided by pharmacodynamically often indifferent medicines, I succeeded in perhaps every case in abolishing the disorders, as tremor, pains, arthralgias, nervous dyspneas, palpitation of the heart, nervous vomiting, limping, etc. Naturally, one must be rather sure of being master of the situation; otherwise, if

the first psychic blow falls very short of its goal and the prediction fails of early realization, the child's trust and faith in the curative force is considerably shaken and the probabilities of a cure by the same physician reduced. In cases of palsy it is often important to prove to the child that he can use his limbs much better than he supposed.

As a last resort — if not used at the first — a more powerful means, impressive through a certain degree of unpleasantness or even painfulness, will find its proper place; as for instance, the faradic current that even in tics, an usually obstinate affection, has proved to be of great curative value. Also cold baths, subcutaneous injections, bitter or disagreeable medicines and other measures of a disagreeable character come here into consideration.

In many instances a method that takes the patient by surprise by its sudden, unexpected application, as for instance, the faradic brush, cold douche, forcible extension of a contracted joint, especially in a changed environment, in the absence of the parents, be it only the office of the physician, finds its indication, particularly in cases of paralysis, contracture, aphonia, etc., or when the intentional neglect failed to create improvement. A strong faradic brush is, in fact, the most persuasive master in such cases. Before the mind of the child, confronting a strange personality and surrounded by a new environment, has had time to find its orientation, or before doubt and criticism could arise, the child overwhelmed at once must have surrendered and the result be obtained. The failure to subjugate the child under the force of suggestion will disclose to him "that he has not yet found his master," and the chances of cure are much diminished. According to the individuality of the child, a peremptory command, if necessary a severe word, may suffice. "The physician lifts up the paralyzed arm and letting it loose, briefly commands: Now keep the arm up" (Bruns).

It will most often be better and safer, instead of using the surprise method, to proceed gradually and slowly; we thereby aim not at the immediate and total, but only at the partial removal of the symptom by our verbal suggestion and encouragement, until within a few days the complete elimination is obtained. Especially may this method be necessary in cases of more severe disturbances in older children, in whom according to the patient's personality the attempt at a complete cure by one stroke might arouse the critical doubt, especially when manifold futile therapeutic measures have already been employed. Of course under all circumstances, any countersuggestive influence, as for instance, the expression of doubt as to the curability by surrounding persons, a careless remark or the aspect of a sick neuropathic

individual must be avoided. It will be left to the physician's experience, ingenuity, discretion and sagacity to decide the kind of procedure in the individual case.

HISTORY OF A CASE OF ASTASIA AND ABASIA

G. K., a girl, aged 11 years, eight days before admission to the Cook County Hospital while retiring felt suddenly that her left leg became weak and gave way and she fell over into her bed. Since then she was bedridden and unable to stand or walk without assistance, dropping forthwith to the floor if not held up. At my first examination, the child's ability while in bed to move the lower extremities with energy, was deliberately dwelt on and suggestively emphasized in the presence of other physicians, as a very good sign of a speedy recovery. She took this as a proof that "her limbs were much better than she had thought." The next day she was able to walk a few steps unsupported, and with encouragement she became, on the third day, able to participate in the plays and running games of the children. No medication.

Psychotherapy is successfully applicable not only in purely and entirely psychogenic diseases, but also for the removal of psychogenic complexes that aggravate or complicate acute and chronic diseases of organic nature, and for the removal of psychogenic residues. They may be very insignificant or in other instances, by their intensity and duration, may far surpass the originally organic symptom, as for instance, the hysterical painful contractures of joints, or abasia and astasia. The recognition of the psychogenic nature of a disturbance by suggesting a possible neuropathic constitution will lead to a therapy that considers the entire individual and treats not merely the symptom, but the patient, employing in addition to the special treatment general measures which have an invigorating effect on the nervous system. It will lead to a pedagogical consideration of the problem and the employment of educational methods that aim at "psychic hardening." The child, too often spoiled, must learn to control his emotions and, subordinating himself to the educator, acquire the inhibitory influences of a well directed will power.

COMMENT

Psychotherapy in childhood particularly gains additional importance in consideration of its applicability as a differential-diagnostic medium in the distinction between neurotico-functional and organic disturbances. Its use, *cum grano salis,* with the point in view of confirming our diagnostic presumption, cannot be overestimated, and its instrumentality is ever emphasized in my teaching at the dispensary. An abundant material for the demonstration of such neurotic cases and their treatment aided substantially in bearing out these claims. A purely psychogenic symptom or residue of an organic disease will with a great degree of certainty be pronouncedly influenced, mostly very soon

cured, or the psychogenic complication from the organic ailment so to speak subtracted, and thus our diagnostic endeavor aided. The diagnostic significance of a striking positive result in an obscure and questionable case, the diagnosis *ex juvantibus* rivals the differential diagnostic value of an effective mercurial cure in lesions suspicious of syphilis.

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HEAD SHAKING WITH NYSTAGMUS IN INFANTS

A STUDY OF SIXTY-FOUR CASES *

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Nomenclature.—Various names have been given to this condition. Those which include the word spasm, such as spasmus nutans, nutatio capitis spastica, gyrospasm, nodding spasm, are objectionable, because it is not a spasm in the sense in which that term is usually used. The terms gyrospasm, rotatory spasm, head nodding and nodding spasm are inaccurate, because the movements may be in any direction. The term spasmus nutans has sometimes led to confusion with the condition known as eclampsia or epilepsia nutans, which is an entirely different disease. Salaam tic, a term sometimes used by French authors, is objectionable because this condition has none of the characteristic features of a tic. Everything considered, head shaking with nystagmus, seems to be the least objectionable name.

Historical.—This condition was first described by Ebert[1] in 1850, and in 1851 by Romberg and Henoch.[2] In 1890 Hadden[3] published two important papers, with a report of twenty-one cases. Caillé[4] of New York was the first to note that when the nystagmatic eye or eyes were bandaged, the movements of the head ceased. In 1897 Raudnitz[5] published his exhaustive monograph on the subject, based on fifteen cases, in which he particularly emphasized the importance of the dark room in the etiology of this condition. In 1911 he published a report on the production of this condition experimentally in young dogs. In England and Scotland, Still[6] and Thomson[7] have reported large series of cases. In this country Peterson,[8] Aldrich,[9] Abt,[10] Judson,[11] Miller,[12] Hamill and Posey,[13] Hill[14] and others have published cases.

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1. Ebert: Charité-Ann., 1850, **1,** 752.
2. Henoch and Romberg: Klin. Wahrnehm. u. Beobact., Berlin, 1851.
3. Hadden: Lancet, London, 1890, **1,** 1293; St. Thomas Hosp. Rep., 1890, **20,** 205.
4. Caillé: Arch. Pediat., 1890, **7,** 171.
5. Raudnitz: Jahrb. f. Kinderh., 1897, **45,** 144; Jahrb. f. Kinderh., 1911, **73,** 259.
6. Still: Lancet, London, 1906, **2,** 207; Clin. Jour, 1906, **29,** 90.
7. Thomson: Jacobi Festschrift, 1900; Brit. Med. Jour., 1901, **1,** 763.
8. Peterson: New York Med. News, 1892, **61,** 374.
9. Aldrich: Am. Jour. Med. Sc., 1899, **177,** 158.
10. Abt: Jour. Am. Med. Assn., 1900, **34,** 269.
11. Judson: Arch. Pediat., 1899, **16,** 197.
12. Miller: Arch. Pediat., 1900, **17,** 561.
13. Hamill and Posey: Am. Jour. Med. Sc., 1904, **128,** 875.
14. Hill: Arch. Pediat., 1911, **28,** 974.

Frequency.—This condition seems to be more common in some countries than in others, if we may judge by the number of reported cases. It is certainly more frequent in large cities. In Budapest at the children's clinic, 15 cases were observed in 3 years among 52,215 patients; in Prague, 8 cases in 2 years among 1,223 patients; in Edinburgh, 35 cases in 11 years among 21,752 patients; in Basel, 2 cases among 6,154 patients; in Christiania 10 cases were seen at the children's clinic in 10 years. The disease appears to be not uncommon in London, Edinburgh, Berlin; and in this country in New York and Philadelphia. During the last 19 years I have had 64 cases under my observation at various children's clinics in New York. The first 15 were seen during 1899, 1900, 1901, at the Good Samaritan Dispensary, chiefly in the service of Dr. Koplik. These figures would indicate that this condition is met with in New York City in about 1 in every 700 infants coming for treatment. The number of cases varies markedly in different years. In 1901 I saw 8 cases; in 1906, 9 cases; in 1910, 13 cases, and in 1918, 7 cases; whereas in some years, 1904, 1908, 1909, 1912, 1914, 1916, no cases were seen. This difference in the prevalence of the disease in different years has also occurred in other cities; for example, in Budapest, in 1891, there was one case in 17,400 patients; in 1894, 9 cases in 16,563 patients. It is relatively somewhat more common among negro children than among white children in New York. In 1910 I saw 10 cases in negro children at the Vanderbilt Clinic. This is probably due to the poor hygienic conditions and the greater prevalence of marked rickets in these children.

Sex.—Females are slightly more frequently affected. In my series, there were 29 males, 35 females. In 133 previously reported cases there were 62 males, and 71 females.

Seasonal incidence.—This condition shows a very distinct seasonal incidence, as shown in the accompanying tabulation.

OCCURRENCE OF HEAD SHAKING WITH NYSTAGMUS BY MONTHS

Previously Reported	Jan.	Feb.	Mar.	Apr.	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.
110 cases ..... Herrman	37	16	10	1	1	1	1	2	4	6	8	23
64 cases ..... Hours sunlight	20	12	6	1	2	0	1	2	2	3	4	8
Edinburgh (Thomson) ..... Hours sunlight	34	57	98	123	165	157	138	145	104	83	47	24
Average, 1911-1917..... New York, Herrman	140	177	223	220	270	288	279	265	243	200	177	151
Mean temperature												
Average, 1911-1917..... New York, Herrman	33.5	29.7	37.2	49.7	60.7	68.3	74.7	72.9	66.4	57.1	44.7	34.4

It will be seen, Figure 1, that it is much more prevalent during the winter months, nearly 70 per cent. of all cases occurring during December, January, and February. The largest number of these begin in January, and recurrences are almost always in this month. As

Thomson has pointed out, the number of hours of sunlight, in temperate climates, is at its minimum during the winter months, Figure 2, and this may bear a definite relation to the prevalence of the condition. It may also account for the very few cases reported in France, Italy, and Spain, for it seems very unlikely that the disease could be overlooked. However, it does not appear probable that the relation is a direct one, and there is no reason to suppose that the amount of sunlight bears a direct relation to this disease. It would be interesting to determine whether head shaking is rare in countries in which there is an unusually large percentage of sunshiny days, for example, New

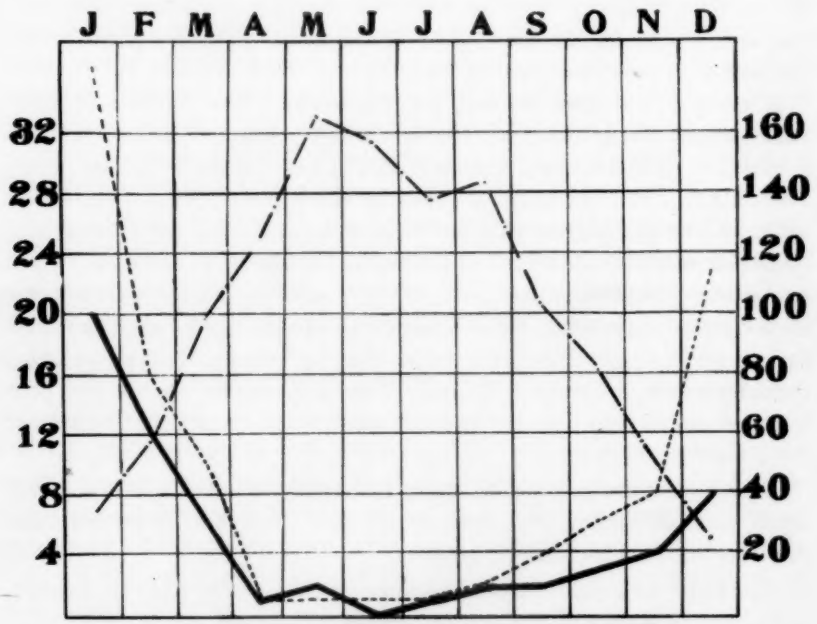

Fig. 1.—Seasonal incidence of head shaking with nystagmus; ———— sixty-four cases observed by the author; — — — — — 110 previously reported; —.—.—. number of hours of sunlight each month in Edinburgh (Thomson).

Zealand, and whether the condition is prevalent in the months of December, January, and February in places in which the summer and winter seasons are different than our own. It will be noted, Figure 2, that the incidence curve of head shaking also corresponds quite closely to the mean temperature curve, so that the temperature might also be important, in so far as during very cold weather the windows would be closed and the infants would not be taken out as much as usual. This may possibly account for the unusually large number of cases seen during the past winter, which was an extremely severe one.

Age incidence.—The disease is most common between 4 and 12 months of age, 75 per cent. of all cases occurring at that time. In my series the age of onset could be definitely determined in 61. It was 1 at 1 month, 2 at 2 months, 2 at 3 months, 2 at 4 months, 3 at 5 months, 8 at 6 months, 8 at 7 months, 5 at 8 months, 5 at 9 months, 6 at 10 months, 4 at 11 months, 6 at 12 months, 2 at 13 months, 3 at 15 months, 1 at 20 months, 2 at 21 months, and 1 at 4 years. The youngest in the series was 1 month old. Schoenberg[15] has also reported a case at that age, and Gee[16] one at 6 weeks of age. After the eighteenth month a first attack is rare, but there may be recur-

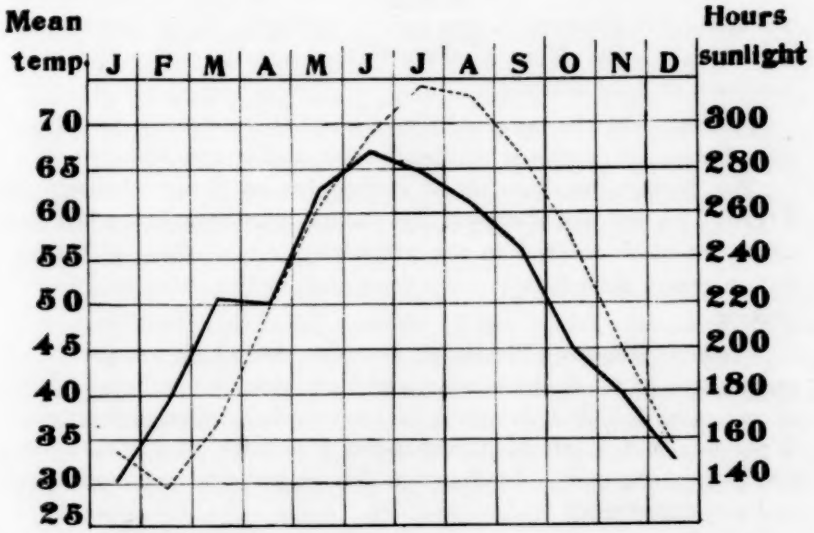

Fig. 2.—New York City, 1911-1917; ———— number of hours of sunlight; — — — — — mean temperature.

rences at that time. In some of the late cases, the original attack may have been overlooked. My oldest patient was 4 years of age. Henoch reported a case of 3 years, Still one of 4 years, and Mowat[17] one of 5 years. It is pretty well established that head shaking is a developmental disease, and that it occurs in certain predisposed infants at a time when the associated movements of the head and eyes are being perfected.

Family history.—In very few of my series, was there a distinct neuropathic family history. In 2 instances the parents were cousins. In 4 cases the mother was extremely nervous, in 3 markedly anemic;

15. Schoenberg: Norsk Mag. f. Lægevidensk., 1891, p. 467.
16. Gee: St. Barthol. Hosp. Rep., 1886, **22**, 96.
17. Mowat: Lancet, London, 1906, **2**, 397.

1 had frequent attacks of migraine; 1 had hysteria. In 5 families one or more of the other children had convulsions; in 1 family one child had epilepsy, and in another family a child died of meningitis. In one instance the condition occurred in twins, and in another family two children were affected. Henoch and Reyher also observed the disease in twins; and Thomson and Hadden have reported instances of more than one case in a family. Three of my cases occurred in mongolian imbeciles. Unlike the latter disease, head shaking does not attack more frequently the first or last child, and it is not more common in families in which there are a large number of children.

Previous history.—In three of my series, the labor was difficult and the delivery instrumental; one was a "twilight" baby, and one was prematurely born. None of these factors seem to play a part in the causation of head shaking.

Feeding.—At the onset of the disease, thirty-five of my patients were breast fed, eighteen artificially fed, and eleven were on mixed feeding, so that the character of feeding has no direct relation to the disease. As one would expect, the rachitic manifestations when present, were more marked in the artificially fed infants, so that to a certain extent such infants were somewhat more predisposed to head shaking.

Previous disease.—Illness, by lowering the vitality, apparently is an etiologic factor in those infants who are already predisposed. Five of my cases followed an attack of bronchitis, 3 followed pneumonia, 6 patients had digestive disturbances, 2 measles, and 1 each nasopharyngitis and otitis. Intercurrent disease tends to increase the head and eye movements.

Teething.—It is to be expected that this condition, which plays such an important etiologic rôle in the minds of mothers, should also be held responsible for head shaking. It would not be surprising if the nystagmus were ascribed to the eruption of the "eye" teeth. Ebert, Henoch, and Still, believe that the eruption of teeth often plays an important part as a source of peripheral irritation. In exceptional cases this may be so, but I have not been able to convince myself that the rôle is an important one. In 18 of my cases the onset of the disease antedated the eruption of teeth. Ebert, who first described the condition, writing in 1850, says, "It is well known that febrile and spastic conditions which are related to the eruption of teeth may antedate the actual appearance of the teeth." If we accept this statement, then anything is possible. I recently saw an infant in whom the eruption of two incisors occurred on the day on which a measles eruption appeared. To the lay mind it seems like cause and effect. In my patients teeth appeared during the course of the disease, but

I never noticed an exacerbation of the symptoms at that time. *Fatigue* does tend to increase the symptoms, so that it is possible that a fretful child that is teething may sleep less, and in that way the head movements might become more distinct. Other sources of peripheral irritation, worms, otitis, etc., have been mentioned as causes, but the evidence is not conclusive.

Trauma. Fall.—In a small percentage of cases this may reasonably be considered an exciting cause in a predisposed child; but it must be remembered that a large number of infants fall and very few show any permanent injury. Only when the head shaking begins shortly after the fall can a relation be claimed; and it is also possible that the fall is a symptom of an already existing coordination neurosis rather than its cause. In six of my series there was a definite history of a fall just preceding the onset of the disease. In one of Hadden's patients two relapses occurred following falls on the head. Peterson[8] says: "Perhaps a concussion of some kind may be found in most of the cases to be the determining factor—a concussion setting up in the centers of the spinal accessory and at times in those of the oculomotor nerves an arrhythmic discharge."

Hygienic conditions, social position, location of rooms.—The hygienic conditions and social position of the family play an important part. Many authors say that the disease does not occur among the well-to-do. This is not absolutely correct, as I have had two cases in families in comfortable circumstances, and Still mentions having seen three such cases. It is rare, however, among this class compared with the frequency with which rickets, laryngismus stridulus, tetany and convulsions occur in them. In large cities, head shaking is more common among those who live in the poorer tenement districts. In my series 11 families lived in the basement, 20 on the first floor, 9 on the second floor, 12 on the third floor, 7 on the fourth floor, and 5 on the fifth or top floor. It will be noted that one half of the families lived in the basement or on the first floor; those living in the basement were not only the poorest, but their rooms were dark and ill ventilated, and the intelligence of the mothers was lower than the average.

Dark rooms.—In 55 of the cases of my series the character of the rooms could be accurately ascertained. I visited nearly all of them myself. It is important to investigate oneself and to determine the exact conditions during the months preceding the onset of the disease. The crib may be placed in a dark corner of a room, not otherwise very dark; the shades may be drawn down a large part of the day so as to darken the room and favor sleep, or the crib may be curtained in order to prevent the light from shining in the infant's eyes. In 40 of my series, the infant was more or less in the dark, and in a

large number of these cases it was necessary to use artificial light in the afternoon during the winter months. In the remaining 15 the room and the spot where the infant lay were fairly light, and in a few of these the room was bright even during the winter months. In several cases, although there was a light room, the infant was kept most of the time in the kitchen, a dark room, so that the mother could watch it while cooking; in several others it was impossible for the mother to take the baby out on account of sickness or the large number of other small children that required attention. On the other hand, in a few cases the mother definitely said that the baby was taken out regularly. It must be remembered that in certain crowded sections of the city a large number of people live in dark rooms, so that only a small portion, probably not more than 1 in 100 infants living in such rooms, contract the disease. Here again we must assume an individual predisposition. The same has been noted in so-called miner's nystagmus; only 3.5 to 4 per cent. of all coal miners working under exactly the same conditions are affected. There can be little doubt that the dark room is an important factor in a large number of the cases of head shaking. During the last eleven years I have seen the same class of patients at the Lebanon Hospital outpatient department in the Borough of the Bronx as I saw during 1899-1902 at the Good Samaritan Dispensary on the Lower East Side of New York. Making due allowance for the difference in the number of patients, the disease was more common in the latter section, principally, I believe, because in the Borough of the Bronx the majority live in rooms which are better lighted and better ventilated. A series of 4 cases of head shaking reported by Rietschel[18] from Finkelstein's service is interesting. On account of the suspicion of communicable disease these 4 infants were transferred from the well lighted ward of the infant asylum to the dark room of a barracks. Shortly after, they developed head shaking. One of the infants was returned to the well lighted and well ventilated ward of the asylum and the head movements soon disappeared. Raudnitz was able to produce experimentally a similar head shaking with nystagmus in puppies by placing them in a dark cage at or very shortly after birth. In from six to eight weeks they developed nystagmus, and after three or four months, shaking of the head. If they were placed in a darkened cage *after* they were 2 months old, these symptoms did not develop. Here again we note, that the causative factors act only at a certain stage in the development of the nervous mechanism which controls the associated movements of the head and eyes. As in infants, at first the nystagmus was only seen

18. Rietschel: Charité-Ann., 1906, **30,** 152. Rietschel refers to John Thomson of Edinburgh, as an American. We should be very glad to claim him.

when the animal looked in certain directions or when the head was held, and the head movements ceased when the eyes were bandaged. If the animals were placed in the open a few days after the nystagmus first showed itself, it disappeared in from one to two weeks, and if they were returned to the dark cage, the nystagmus reappeared in from two to seven days. If the animal was kept in the dark, however, so that the nystagmus persisted for several months, it required as much as nine months' exposure to daylight to cause the nystagmus to disappear. The examination of the fundus, the vision, and the microscopic examination of the brain and retina of the affected animals showed no pathologic changes. It is worth noting that in Raudnitz' experimental work on animals the cage was dark and apparently there was no artificial light to which the eyes of these young animals was attracted. In explaining the causation of the condition in infants he laid stress on the straining of the eyes in looking at an artificial light some distance above the level of the head. Raudnitz believes that the nystagmus associated with the head shaking in infants is analogous to that observed in coal miners.[19] Although there are some points of analogy, there are some objections to this theory. The nystagmus of coal miners seems to be due to the strained position of the head, eyes, and body of the men, working in a place which is imperfectly lighted. The darkness alone is not sufficient, for this form of nystagmus occurs *only* in *coal* miners. The strained position of the head and eyes alone is not sufficient, for it does not occur in ceiling painters, and in others who have to look more or less constantly upward. A large percentage of the miners affected have errors of vision, while the infants with head shaking associated with nystagmus have no such error. The nystagmus of miners is usually bilateral and conjugate; that of the infants is usually unilateral, or is much more marked in one eye, and is frequently not conjugate. In miners head movements are uncommon and are only present in severe cases; in infants head movements are the rule. In miners the head movements do not cease when the eyes are bandaged as they do in the infantile form.

Rickets.—Kassowitz,[20] Hochsinger[21] and Stamm[22] consider the head shaking of infants a rachitic manifestation. In my series, 45, or 70 per cent., of the patients showed some manifestations of this disease. This is about twice as frequent as in other infants brought for treatment. Thomson's figures are 94.2 per cent. rickets in the affected infants, 46.9 in other infants. Of course the percentage of rickets

19. Nieden: Nystagmus der Bergleute. Wiesbaden, 1894.
20. Kassowitz: Vorles. u. Kinderk. im alter d. Zahnung, Vienna, 1892, p. 165.
21. Hochsinger: Verhandl. d. Gesellsch. f. Kinderh., 1897, **14**, 238.
22. Stamm: Arch. f. Kinderh., 1902, **32**, 259.

will vary according to the clientèle. For example, in New York City, rickets is much more common in negro children, so that it is not surprising that every one of my 10 cases of head shaking in negro children showed distinct rachitic changes.[23] However, in 19 of my cases rickets was not present, so that it cannot be an indispensable factor. Several other points indicated by Thomson are of interest. In head shaking, antirachitic treatment is not followed by the rapid improvement which we are accustomed to see in rickets. This has been my own experience and is contrary to that of Stamm, who noted distinct improvement in the head shaking *in a few weeks.* Cases of head shaking are rarely associated with laryngismus stridulus, facial irritability, tetany or convulsions. In my series, although many had marked rachitic manifestations, only 3 had laryngismus stridulus and facial irritability, and in Thomson's 35 cases only 2 had laryngismus stridulus and facial irritability. There does not seem to be a distinct relation between the frequency of laryngismus stridulus and head shaking in a given locality. In Vienna, Kassowitz in six years saw 370 cases of laryngismus stridulus, that is on the average 61 cases a year; in Edinburgh, Thomson in three years saw only 61 cases, that is, 20 a year. On the other hand, Kassowitz in eight years saw only 9 cases of head shaking; that is, about one a year, while Thomson saw 35 cases in eleven years; that is, 3 a year. If these conditions were due, as Kassowitz supposes, to the increased vascularity of the bones of the skull and the neighboring tissues, then we should expect that head shaking would be frequently present in rachitic infants with craniotabes; however, such is not the case. Rietschel tested the electrical reactions in 4 cases of head shaking, and 3 of the 4 gave normal reactions. While head shaking is rare in well-to-do families, rickets, laryngismus stridulus, tetany, and convulsions are not uncommon. As is well known, rickets involves not only the bones, muscles and ligaments, but the central nervous system as well, so that it is not surprising that a rachitic infant should be somewhat more predisposed to the development of a functional neurosis.

Pathogenesis.—Notwithstanding the great amount of investigation on this subject, the exact explanation of the disturbance of the nervous mechanism which results in the head and eye movements is still something of a puzzle. The solution requires the combined investigation of the pediatrist, neurologist, and ophthalmologist. Thomson says:

> The nervous mechanism whose function is at fault is evidently that which includes the semicircular canals in its circuit, and which regulates the coordination of the movements of the eyes with those of the head. Dr. Alex Bruce tells me that the nucleus of Deiters (one of the end nuclei of the vestibular

23. Herrman: Arch. Pediat., 1910, **27,** 370.

nerve, lying at the lateral angle of the fourth ventricle) is in all probability the seat of the disturbance. He infers this from its connection with the oculomotor nuclei and with the anterior cornua of the cord.

Henoch had about the same in mind when he wrote:

The frequent combination of head shaking with nystagmus is interesting, as it indicates that the nuclei of the spinal accessory and the upper spinal nerves which supply the affected muscles of the head and neck, are in close relation to those of the eye muscles.

The most satisfactory explanation of the pathogenesis of this condition is that originally suggested by Hadden and later modified and amplified by Mills[24] and Aldrich. Mills says:

Hadden believes that the symptoms point to an instability of the motor centers above the nuclei in the spinal cord and fourth ventricle, and he would therefore attribute the disorder to a functional or other disturbance of the cerebral cortex. The child has acquired certain voluntary or purposive movements of the head and eyeballs, but these have not as yet become thoroughly organized and fixed in the psychomotor areas of the brain, hence a dissolution takes place because of the instability of the strained cortical centers to stand the work to which they have been too early subjected.

Aldrich amplifies this as follows:

The writer in considering the pathology of these cases accepts as a fact the obvious relation of the head and eye movements, hence we have to consider an automatic head and eye movement in a child of unstable nerve development, and at an age in which the associations of those necessary movements are being educated and fixed in the psychomotor areas of the brain. Anyone that has observed the head and eye movements of the infant cannot have failed to mark the incoordinated attempts at associated movements of the head and eyes. The fibrous connection between the visual areas of the cerebral cortex and the fovea centralis that is necessary to perfect vision does not fully develop until after birth, and only gradually becomes medullated and fit for function. After this process is completed, which takes place only when the cortical cell has attained a degree of maturity that provides ample nutrition for its axis cylinder, then the structural and physiologic integrity of the central neuron is complete. During this time the same process of development in the peripheral neuron is going on with even greater rapidity, and we have the beginning of one of the most wonderful and mysterious processes of the nervous system—the communication between the central and peripheral neuron. . . . Binocular adjustment, judgment of fixed objects, spatial relations, including station, are acquired by the child as the medullation progresses. If this progress of medullary development of the nerve supply of the eyes is either interfered with by disturbance of nerve nutrition or rendered functionally imperfect through early acquired opacity of the refracting media, or by congenital absence of a place in the retina that has more acute and perfect vision than elsewhere (fovea centralis), or a congenital defect in the receptive center in the cortex, or an exhaustion of any of that delicate apparatus, then we are liable to get a rapid to and fro movement of the eyes—nystagmus.

Symptoms. Movements of the head.—The movement of the head is usually the first manifestation noticed by the mother, but in a

24. Mills: Am. Textbook Dis. Child., Ed. 2, 1894, p. 712.

certain number it may be preceded by a peculiar "cocking" of the head to one side. In some the nystagmus may precede the head movements but may not be noticed because it is present only when the child looks in certain directions, or when the head is held. The muscles chiefly affected are the sternocleidomastoid, the trapezius and the rectus capitis. The movements are regular and rhythmical and from 60 to 100 a minute. Usually they are not continuous, but come on at longer or shorter intervals. The direction is rarely purely horizontal, vertical or rotary, but when primarily horizontal, slightly upward to one side and downward to the other, the excursions often being greater to one side. If primarily vertical, it is rarely a pure nod forward and backward. The movement may be a combination of the horizontal and vertical, and they may be in different directions at different times. In my series the movements were primarily horizontal in 44, vertical in 12, rotary in 4, and horizontal or vertical at different times in 4. The movements are often more distinct when the child is angry or fatigued, and during an attack of some intercurrent disease. They cease when the child is lying down and in sleep. There is, however, an occasional exception to this rule; for example, in one of my cases, in which the movements were unusually frequent and well marked, they continued when the child was lying down, and Amberg[25] also mentions a case in which the movements continued during sleep. It was first noticed by Caillé, and later by Raudnitz, that the movements of the head ceased when the eyes were bandaged. It is not possible to test this in all patients, because some object so strongly that the movements of the head due to anger prevent the drawing of definite conclusions; but in 14 of my cases, I was able to corroborate this statement. The movements of the head are best seen when the infant is gazing in the distance and is not interested in any particular object. If an object is brought within a short distance, so that it is definitely fixed, the movements of the head cease.

Movements of other parts of the body.—I have not observed movements of the extremities, such as described by Thomson, Still, and others, or of the trunk, as reported by Hadden. Ausch[26] noticed in one of his cases movements of the hands, as if the child was vexed. I have frequently seen such movements in infants who were entirely free from head shaking.

The peculiar position of the head.—(Fig. 3).—About one-half of these patients have a peculiar way of "cocking" the head to one side and looking out of the corners of the eyes. This may precede the head movements and may persist after these movements have ceased. In

25. Amberg: Arch. Pediat., 1901, **18,** 831.
26. Ausch: Arch. f. Kinderh., 1900, **28,** 161.

75 per cent. of the infants in whom this "cocking" was present the head was inclined to the left. This is noteworthy in connection with the fact that in sixteen of the twenty-three cases in which the nystagmus was unilateral, the left eye was affected. Some of the patients have a habit of looking down with a coy expression; others throw the head back and look out of the partially closed lids.

Movements of the eyes.—The nystagmus may appear before, simultaneously with or after the head movements. It may persist after the head shaking has ceased. In 35 of my cases the nystagmus was bilateral, in 23 unilateral. Of the latter, 16 affected the left eye, 7 the right eye. Even when the nystagmus was bilateral, it was frequently more marked in one eye. In 6 cases the nystagmus was not seen when the patients were examined in the ordinary way, but it is known that in some cases the nystagmus is so slight that it can only be detected by an ophthalmoscopic examination. The direction of the

Fig. 3.—Peculiar cocking of the head seen in infants affected with head shaking with nystagmus.

nystagmus is often not purely horizontal, vertical or rotary; it may be different in the two eyes, or when the patient looks in different directions. In the 58 cases in my series in which nystagmus was present, it was primarily horizontal in 36, vertical in 6, and rotary in 15; in the remaining case it was impossible to determine the direction. The movements of the eye are much more rapid than those of the head, about 200 to 300 a minute. The nystagmus is increased by holding the head, and is more distinct when the child looks in certain directions, usually when it looks upward and to the right, when the right eye is affected, and upward and to the left, when the left eye is affected. It is also more distinct when the child fixes an object at a short distance, and when the eyes are converged. It is not present during sleep, as I was able to determine in several infants that I examined. When the nystagmus is bilateral it is not necessarily conjugate. According to Thomson,[7] it differs from other forms in that

the pupils alternately approach and recede. Spicer[27] was not able to verify this in all of his cases. Thomson also says that in rotary nystagmus the center of the pupil does not describe a circle, but an ellipse or an irregular figure. The movements of the head are not simply compensatory to those of the eyes, for the rate is different, and the two are not necessarily in the same direction; for example, the movements of the head may be vertical, while those of the eyes are horizontal. The nystagmus may persist after the head movements have ceased, and it may recur without the appearance of head movements. In exceptional cases the nystagmus may be the only manifestation. Such cases may be regarded as atypical or incomplete. In 4 of my series, convergent strabismus was present; in 3 there was hippus; 3 had associated movements of the upper lids, "nictitation;" and in 2 there was some sensitiveness to light; 12 of my patients were examined by ophthalmologists, and none of these showed any changes in the fundus, defects of vision or opacities in the media. Similar examinations reported by other authors were also negative, except that in two of Hadden's cases the fundus was light colored, and in one a slight crescent of atrophy was present around the left disk. In a few of my patients, I instilled homatropin in order to paralyze accommodation. The nystagmus was diminished, but the head movements continued. This is what one would expect, for as previously mentioned, the head movements cease when an object is distinctly seen and fixed; by paralyzing accommodation this becomes impossible. As nystagmus is sometimes associated with disturbances in the semicircular canals, Raudnitz had the ears examined in several cases. None showed any lesions, and syringing of the ears had no especial effect on the nystagmus.

Associated conditions. — In my series, 6 patients were anemic, 5 had an enlarged spleen, 2 tuberculous lesions, 2 papular urticaria, 2 eczema, 3 a geographical tongue, 1 blepharitis ciliaris. One child had attacks of apnea. Hadden reports cases with attacks of unconsciousness, partial or complete, and convulsions. Such cases are rare, and the more severe probably represent cases of so-called epilepsia nutans.

Duration.—The condition seldom lasts less than 2, or more than 12 months. In my series, the duration of 50 cases could be determined. In 6 it was 3 months; in 6 it was 4 months; in 12 it was 5 months; in 6 it was 6 months; in 4 it was 7 months; in 4 it was 8 months; in 2 it was 9 months; in 4 it was 10 months; in 6 it was 12 months. In 3 there was a recurrence during the following winter, 2 in January and 1 in February. In exceptional cases, however, the disease may last for more than one year. Spicer mentions a case in

27. Spicer: Brit. Med. Jour., 1901, **1**, 1120.

which it was present at 4½ years of age; and another in which the nystagmus persisted at 13 years of age.

Subsequent history.—I have been able to follow 15 of my cases for a period of from two to ten years. Of these, 8 had no subsequent disease that had any relation to the head shaking. Of the remaining 7, 2 had enuresis, one of these until she was 6 years of age; 1 had convulsions; 1 pavor nocturnus; 1 a facial tic; 1 was extremely sensitive and also anemic; and 1 was a very restless sleeper and had grinding of the teeth. With the exception of the 3 cases in mongolian imbeciles, all the children showed a normal average mental development. I recently saw a girl of 13 years with a mild type of exophthalmic goiter (Graves' disease) who had had head shaking in infancy. In none of the 5 children who were followed to the eighth year did chorea develop. This is of some interest, as several authors have thought that there was a possible relation between these two diseases.

Diagnosis.—The principal features of this condition are so characteristic that the correct diagnosis is seldom difficult. Some of the earlier authors confused it with *eclampsia* or *epilepsia nutans,* which is really an epileptic equivalent. This disease occurs in attacks, and is associated with partial or complete unconsciousness. There is no nystagmus. In head shaking there are no sudden attacks, the movements are more or less continuous, and consciousness is not lost. The movements in head shaking are entirely different from those of a *tic* or *habit spasm.* They are smooth, regular, and rhythmical, not jerky. Tics do not occur at such an early age, and they are not associated with nystagmus. The *rocking* movements of the trunk and head, frequently seen in infants and young children, have only a remote resemblance to head shaking. The movements are voluntary, and even when they are not a manifestation of masturbation, seem to give the patients a certain amount of pleasure or satisfaction. Nystagmus is absent. Head shaking has occasionally been confused with the nocturnal movements of the head, *Jactatio capitis nosturnia,* which is sometimes seen in older children. These movements differ from the head shaking of infants in that they occur during sleep, or at least in a subconscious state, and are not associated with nystagmus. *Head rolling,* like head shaking, is seen in rachitic infants, but it is only present when the child is lying down; it is a voluntary act, and it is not associated with nystagmus. There is a rare form of *congenital head shaking with nystagmus* which is due to pathologic changes in certain areas of the brain. This condition as well as a number of other diseases of the central nervous system, associated with head movements or nystagmus, can easily be differentiated from the benign head shaking of infants, by the fact that the disease is progressive and

persists throughout life. In all these conditions when nystagmus is present it is bilateral and conjugate.

Prognosis.—Head shaking with nystagmus in infants is a benign disease; all patients recover. The mothers may be assured that this disease will not interfere with the general health, or with the future mental and physical development of the child. The disease usually begins in the winter months and disappears during the following summer. Occasionally there is a recurrence of symptoms the following winter, but this also is of short duration. A few of the patients show a neuropathic tendency in later childhood.

Treatment. — The general condition, the hygienic surroundings, should be improved if possible. The room should be light, and the patient should be kept in the open air as much as possible. In several of my cases the mother noticed that there was a rapid improvement when the child was taken to the country. If there are any sources of peripheral irritation, these should be removed; if there are digestive disturbances, the diet should be regulated. Those infants that present rachitic manifestations should receive phosphorus and cod liver oil. In most cases this treatment is sufficient. I have not seen any marked improvement following the administration of bromids, belladonna or arsenic.

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THE EFFECT OF INJECTIONS OF PITUITARY SOLUTION ON THE URINARY OUTPUT IN A CASE OF DIABETES INSIPIDUS*

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The striking relief of symptoms in diabetes insipidus on injection of extracts of the posterior lobe and pars intermedia of the hypophysis cerebri has been known for some years, but no adequate explanation for the effect has yet been offered. Therefore, any new facts bearing on the action of pituitary solution should be made known.

A boy of 9½ years suffering from diabetes insipidus was studied in the St. Louis Children's Hospital in March, 1918. Attention is called to one of the results of this study. Injections of pituitary solution checked the rate of output of water and chlorids invariably; but checked the rate of output of urea, creatinin and uric acid little or none at all. The significance of this difference is not clear. Further study from this standpoint should be directed to other cases of diabetes insipidus, and to normal persons in whom artificial polyuria has been induced by the ingestion of large quantities of water; and to the other urinary constituents, in order to discover whether the excretion of electrolytes in general is hindered by the action of pituitary solution, while the excretion of nonelectrolytes in general is unaffected.

From a therapeutic standpoint, it may be said that this case showed the well known relief of symptoms when pituitary solution was given. There seemed to be no harmful effect from repeated injections, and it was considered practical to have this treatment continued at home.

REPORT OF CASE

M. G., a boy, aged 9½ years, was admitted to the St. Louis Children's Hospital, Feb. 23, 1918 (Case 12474), with a moderately severe case of diabetes insipidus and with the complaint that he drank lots of water and passed a large amount of urine.

Family History.—His father and mother were well. A brother of 11 years and a sister of 15 years were well. There have been no miscarriages and there was no history of tuberculosis in the family.

Past History.—The child was delivered spontaneously at term and was nursed one year. He had measles and pneumonia at 11 months. His tonsils and adenoids were removed at 6 years. He has had a divergent squint since birth and is very bright at school.

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Present Illness.—This began in August, 1917, with great thirst and copious urine. He is said to have passed 12 quarts a day. Has lost some weight and become pale and weak lately. His sleep has been disturbed by the pollakiuria. No other symptoms have been noted. Treatment so far has not helped him.

Physical Examination.—He was a well developed, bright boy of perfectly normal appearance, excepting for an external strabismus. The viscera were normal and there were no signs of endocrine disorder. The neurologic examination was negative, including the ophthalmoscopic examination. Pulse and temperature were normal.

Laboratory Examinations.—Blood: red blood cells, 4,566,000; white blood cells, 9,600; polymorphonuclears, 68 per cent.; hemoglobin (Sahli), 75 per cent.; urea nitrogen, 10.4 mg. per 100; normal protein nitrogen, 32.7 mg. per 100; plasma sodium chlorid, 0.625 per cent.; plasma carbon dioxid, 49.8 volume per cent. Wassermann reaction negative.

Phenolsulphonephthalein excretion: 52 per cent. first hour, 19 per cent. second hour; two hours, 71 per cent.

Lumbar puncture: Clear spinal fluid under no increase of pressure, 5 cells per cubic millimeter. Globulin test negative (Noguchi); Wassermann test negative.

Complement fixation test for tuberculosis was positive in serum; the von Pirquet test was slightly positive. Roentgenogram of the chest was negative. No signs of tuberculosis were discovered. Roentgenogram of the skull revealed slight convolutional atrophy; sella turcica normal.

Urine: Pale, from 6 to 7 liters per day, specific gravity from 1.001 to 1.003, no albumin, sugar, casts or cells.

EXPERIMENTAL

The patient was kept in bed for three days; for the remainder of the time, he was in a wheel chair during the day. His fluid intake was measured by the nurse in charge. On two occasions, he took water without permission. His diet was that given the other patients excepting that he had "salt-free" articles, March 2 and 3; and a specially prescribed and weighed diet, March 14 and 17.

Urine was collected in quart bottles from 6 a. m. to 6 a. m., and preserved under toluene in the refrigerator. The analytic methods were as follows:

Urea was determined by Marshall's method.[1] *Chlorids* were determined by Van Slyke and McLain's method, and expressed as "sodium chlorid."[2] *Creatinin* was determined by Folin's method.[3] *Uric acid* was determined by Folin's method.[4] *Calcium* was determined by Lyman's method.[5] *The acidity* was determined by titrating the diluted urine (usually diluted 1:10) with fiftieth-normal hydrochloric acid or sodium hydroxid, for neutrality with phenolsulphonephthalein as indicator. The results are expressed in cubic centimeters of tenth-normal acid or alkali. This method, of course, gives relative values only.

1. Marshall, E. K.: Jour. Biol. Chem. 1912-1913, **14,** 283.
2. Van Slyke, D. D., and McLain, F. C.: Jour. Biol. Chem. 1915, **21,** 361.
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PITUITARY SOLUTION

The preparation known as surgical pituitrin was purchased from Parke, Davis and Company. It is said to possess about twice the activity of the obstetrical pituitrin. It represents the active constituents of the posterior lobe and pars intermedia of the pituitary glands of the ox. No disagreeable effects were produced on the patient, although he experienced a desire to defecate soon after the injections. No elevation in blood pressure followed the injections.

CLINICAL RESULTS OBTAINED

The effect of various procedures on the fluid intake and urinary output is shown in Table 1.

TABLE 1.—SUMMARY OF DAILY URINE VOLUME IN CASE OF DIABETES INSIPIDUS TREATED WITH PITUITRIN

Date	Intake	Output			Pituitrin	Water
		Day	Night	Total		
2/27-28	2,450	1,714	940	2,654	.....	Voluntarily limited
3/1-2	6,050	3,110	1,520	4,630	.....	Not limited
3/2-3	6,750	3,565	2,835	6,400	.....	Not limited
3/3-4	6,675	3,875	2,735	6,610	.....	Not limited
3/4-5	2,825	2,106	450	2,556	0.5 c.c. hypodermically at 10:30 a.m.	Not limited
3/5-6	2,300	1,189	950	2,139	0.5 c.c. hypodermically at 7:30 a.m.	Not limited
3/6-7	2,650	1,667	470	2,137	0.5 c.c. hypodermically at 7:30 a.m.	Not limited
3/7-8	2,600	2,767	960	3,727	.....	Not limited
3/8-9	1,273	870	910	1,782	1 c.c. hypodermically at 7:30 a.m.	Not limited
3/9-10	4,575	3,790	1,680	5,470	.....	Not limited
3/10-11	3,000	3,720	2,000	5,720	1 c.c. by mouth at 10 a.m.	Not limited
3/11-12	3,585	3,747	2,000	5,747	2 c.c. by mouth at 10 a.m.	Not limited
3/12-13	1,950	1,303	370	1,673	0.25 c.c. hypodermically at 10 a.m. and 6 p.m.	Not limited
3/13-14	3,850	2,205	1,900	4,105	0.25 c.c. hypodermically at 8 a.m.	Forced in day
3/14-15	5,500	2,637	2,760	5,397	0.25 c.c. hypodermically at 9:45 a.m.	Forced in day
3/15-16	5,600	2,151	2,383	4,536	0.25 c.c. hypodermically at 10:45 a.m.	Forced in day
3/16-17	4,250	2,143	2,060	4,203	0.25 c.c. hypodermically at 10:30 a.m.	Forced in day

By strong voluntary effort, the patient succeeded in ingesting only 2,450 c.c. of water on February 27. His urine measured 2,654 c.c. This is much less than the intake and output on the next three days, when his fluid intake was not limited. A low salt diet did not diminish the output on March 2 and 3 and March 3 and 4.

On the morning of March 4, 0.5 c.c. of surgical pituitrin was injected subcutaneously in the region of the right deltoid. A very

striking reduction of urine occurred. At the same time, thirst also diminished. The effects of pituitrin injections are similiar on the days following. It is especially to be noted that the patient's night urine was much lessened so that he awoke but once or twice to void.

On March 7, no pituitary solution kas given; the output rose to 3,727 c.c., or less than the usual level. This favorable effect of pituitary solution, persisting more than twenty-four hours, does not always occur, as is shown on March 9 and 10, when the output was 5,470 c.c., following the injection of 1 c.c. the day before.

TABLE 2.—HOURLY OUTPUT OF URINE ON A SINGLE DAY AS INFLUENCED BY 0.5 C.C. PITUITARY SOLUTION INJECTED AT 10:45 A. M. INCREASE OF SPECIFIC GRAVITY, AND DECREASE OF WATER AND CHLORID OUTPUT

Time	Volume, C.c.	Specific Gravity	Urea Nitrogen		Sodium Chlorid	
			Per Cent.	Grams	Per Cent.	Grams
6- 7 a. m.	285	1.004	0.073	0.21	0.13	0.37
7- 8 a. m.	385	1.003	0.078	0.30	0.083	0.31
8- 9 a. m.	365	1.004	0.095	0.35	0.092	0.35
9-10 a. m.	310	1.004	0.089	0.27	0.10	0.31
10-11 a. m.	270	1.003	0.073	0.20	0.09	0.24
11-12 a. m.	24	1.012	0.708	0.17	0.15	0.036
12- 1 p. m.	36	1.009	0.63	0.23	0.19	0.069
1- 2 p. m.	49	1.011	0.35	0.17	0.17	0.083
2- 3 p. m.	74	1.011	0.56	0.41	0.17	0.128
3- 4 p. m.	104	1.010	0.05	0.05	0.17	0.18
4- 5 p. m.	104	1.009	0.31	0.32	0.19	0.20
5- 6 p. m.	100	1.009	0.017	0.02	0.24	0.23
Day.....	2,106	....	0.128	2.70	0.12	2.61
Night.....	450	1.010	0.14	2.80	0.076	0.34
Total.....	2,556	....	0.129	5.50	0.113	2.95

Given by mouth in this case, the pituitary solution was quite inactive up to doses of 2 c.c.

When pituitary solution was injected in two doses of 0.25 c.c. each, the effect was more striking than when given in a single dose of 0.5 c.c. This method of divided doses is more necessary in cases of greater severity than in such a case as the present one.

When the fluid intake is forced to a level about twice as great as the patient would choose, and pituitary solution is injected in the

morning, the day output is somewhat lowered, while the night output rises to compensate for the intake.

More detailed studies of the effects of injections of pituitary solution are presented in the series of tables. Two hourly or one hourly specimens of urine were collected from 6 a. m. to 6 p. m., with a single night specimen, from 6 p. m. to 6 a. m. The injections were usually made about 9 or 10 a. m. In this way, one has two or four hourly specimens of urine before an injection, in order to establish a level of urinary excretion; and a fairly long period after the

TABLE 3.—Two-Hourly Output of Urine for Three Days; no Pituitary Solution Being Given. Variations in Urea and Chlorid Output. Total Output not Lessened by Low Salt and Nitrogen Diet

Time	Vol.	Urea N	NaCl	Vol.	Urea N	NaCl	Vol.	Urea N	NaCl
6- 8 a. m.	755	1.16	0.725	430	0.602	0.179	610	0.587	0.595
8-10 a. m.	590	0.89	0.579	520	0.388	0.156	670	0.556	0.506
10-12 a. m.	300	0.56	0.257	640	0.825	0.196	810	0.382	0.745
12- 2 p. m.	660	0.99	0.341	735	0.902	0.268	600	0.825	0.505
2- 4 p. m.	670	1.61	0.657	410	0.399	0.254	630	0.662	0.547
4- 6 p. m.	195	0.27	0.123	830	0.621	0.403	555	0.514	0.274
Day.....	3,110	5.48	2.68	3,565	3.80	1.46	3,875	3.53	3.17
Night.....	1,520	3.27	4.74	2,835	3.97	1.95	2,735	2.73	1.10
Total.....	4,630	8.75	7.42	6,400	7.79	3.41	6,610	6.26	4.27
Date.....	March 1-2			March 2-3			March 3-4		
Diet.....	Regular			Low Salt			Low Salt		

injection to observe its effects. No special effort was made to restrict the fluid intake.

Table 2 shows the result of injecting 0.5 c.c. of pituitary solution at 10:30 a. m., March 4. Before the injection the hourly output of urine is high, and fairly constant, of low fixed specific gravity and low sodium chlorid and urea concentration. Following the injection, there is, ***within half an hour***, much more concentrated urine, of higher sodium chlorid and urea content, and of only about one-eleventh the volume per hour. The effect slowly disappears, but is evident throughout the remainder of the day.

When one considers the actual quantity of urea and chlorid excreted per hour, one sees a striking difference. Whereas, the actual amount of urea excreted per hour is only slightly affected by the injection of pituitary solution, the amount of chlorid excreted per hour is considerably reduced for several hours. On other days, Table 4, the suppression of chlorid excretion is always to be found; sometimes, but not

TABLE 4.—HOURLY OUTPUT OF URINE FOR THREE DAYS AS INFLUENCED BY INJECTIONS OF PITUITARY SOLUTION

Time	Vol.	Urea N	NaCl	Creatinin	Vol.	Urea N	NaCl	Creatinin	Vol.	Urea N	NaCl	Creatinin	Uric Acid
6- 7 a.m.	285	0.207	0.366	21.1	145	0.257	0.381	29.0	262	0.411	0.697	52.0	62.4
7- 8 a.m.	385	0.302	0.314	23.5	132	0.081	0.359	17.0	182	0.238	0.495	17.8	48.3
8- 9 a.m.	365	0.347	0.349	23.2	20	0.010	0.049	8.8	37	0.167	0.079	15.4	41.0
9-10 a.m.	310	0.269	0.313	18.5	2	.....	.....	....	40	0.243	0.142	17.3	42.7
10-11 a.m.	270	0.197	0.243	14.7	70	0.102	0.244	28.0	54	0.382	0.210	23.7	54.6
11-12 a.m.	24	0.171	0.036	12.3	50	0.051	0.163	14.5	70	0.263	0.255	17.1	36.2
12- 1 p.m.	36	0.227	0.069	13.3	70	0.069	0.192	16.0	95	0.405	0.365	23.5	40.4
1- 2 p.m.	49	0.173	0.083	16.0	100	0.148	0.211	16.0	230	0.504	0.850	31.5	66.3
2- 3 p.m.	74	0.414	0.128	22.1	156	0.131	0.342	20.3	295	0.767	0.849	36.3	
3- 4 p.m.	104	0.052	0.176	29.2	158	0.160	0.321	19.0	2				
4- 5 p.m.	104	0.322	0.195	18.4	156	0.181	0.220	17.2	205	0.586	0.551	26.5	
5- 6 p.m.	100	0.017	0.232	23.8	130	0.066	0.143	16.9	195	0.727	0.622	29.6	
Day.....	2,106	2.70	2.50	227.0	1,189	1.28	2.63	208.0	1,667	4.70	5.12	291.0	
Night.....	450	2.80	3.42	167.0	950	1.39	1.76	172.0	470	1.26	1.80	159.0	
Total.....	2,556	5.50	5.92	394.0	2.139	2.67	4.39	375.0	2.137	5.96	6.92	450.0	
Date.....	March 4-5				March 5-6				March 6-7				
Diet.....	Low Salt				Regular				Regular				
Pituitrin..	0.5 c.c. hypodermically at 10:45 a.m.				0.5 c.c. hypodermically at 8:45 a.m.				0.5 c.c. hypodermically at 8 a.m.				

as a rule, the urea excretion is also diminished. Irregularities of this sort may be dependent on other factors, such as food intake. The results of analyses made when no pituitary solution is given are shown in Table 3.

It was thought that the rate of elimination of creatinin and uric acid might be less influenced by food ingestion than that of urea.

The output of these substances as influenced by the injection of pituitary solution is only moderately hindered (Table 4).

FURTHER OBSERVATIONS

In order to further study the effect of injections of pituitary solution on the output of water, salts, and nitrogen, the rates of intake of these substances were made practically constant. For three days

TABLE 5.—HOURLY OUTPUT OF URINE AS INFLUENCED BY PITUITARY SOLUTION WHEN WATER WAS FORCED—150 C.C. EVERY HALF HOUR FROM 6 A. M. TO 6 P. M., AND WHEN CHLORIDS WERE FORCED, 1 GM. EVERY HOUR FROM 6 A. M. TO 6 P. M.; 0.25 C.C. OF PITUITARY SOLUTION GIVEN AT 9:45 A. M.

Time	Vol.	Sp. Gr.	Urea N		NaCl		Creatinin		Uric Acid		Calcium	
			%	Gm.	%	Gm.	Mg.*	Mg.	Mg.*	Mg.	Mg.*	Mg.
6- 7 a.m.	345	1.005	0.085	0.29	0.25	0.86	7.2	24.8	4.6	16.0	2.8	9.8
7- 8 a.m.	370	1.004	0.074	0.27	0.19	0.70	6.9	25.3	5.1	19.0	2.8	11.0
8- 9 a.m.	330	1.005	0.078	0.26	0.20	0.65	7.2	24.1	5.0	17.0	3.6	12.0
9-10 a.m.	315	1.003	0.068	0.21	0.12	0.36	7.2	23.0	4.9	16.0	2.3	7.2
10-11 a.m.	165	1.017	0.27	0.04	0.45	0.07	47.6	7.9	3.3	5.4	1.3	2.1
11-12 a.m.	47	1.013	0.34	0.16	0.47	0.22	40.0	19.0	2.5	12.0	1.2	5.5
12- 1 p.m.	58	1.017	0.41	0.24	0.64	0.36	43.7	25.0	2.7	16.0	1.0	6.1
1- 2 p.m.	60	1.014	0.25	0.15	0.45	0.27	27.7	17.0	2.2	13.0	5.5	3.3
2- 3 p.m.	140	1.006	0.20	0.28	0.25	0.35	15.5	22.0	1.1	15.0	3.3	4.6
3- 4 p.m.	200	1.007	0.12	0.24	0.30	0.59	9.3	19.0	6.1	12.0	6.7	7.4
4- 5 p.m.	480	1.008	0.071	0.34	0.22	1.05	4.8	15.0	2.8	14.0	4.4	21.0
5- 6 p.m.	275	1.005	0.056	0.15	0.16	0.43	4.0	11.0	2.9	7.6	4.1	11.0
Day.....	2,637	....	0.10	2.63	0.22	5.91	8.8	23.3	6.2	163.0	3.8	101.0
Night.....	2,760	.....	0.058	1.60	0.22	6.07	8.3	230.0	5.4	150.0	4.8	133.0
Total.....	5,397	.....	0.078	4.23	0.22	11.98	8.6	463.0	5.8	313.0	4.3	234.0

* Milligrams per 100 c.c.

the patient received a measured diet, which contained from 3.9 to 4.3 gm. of nitrogen and 2 gm. of sodium chlorid per day; he was induced to drink 150 c.c. of water every half hour from 6 a. m. to 6 p. m.

On the first day, he received in addition, 1 gm. of sodium chlorid, given in water, every hour from 6 a. m. to 6 p. m. Pituitary solution, 0.25 c.c., was injected at 9:45 a. m. As before, the volume of urine is strikingly diminished for from 4 to 5 hours after the injection of

the pituitary solution. The rate of salt output before injection is about 0.64 gm. per hour; for five hours after injection, it averages 0.25 gm. per hour. The rate of urea nitrogen excretion falls from 0.25 gm. per hour to 0.16 gm. per hour; creatinin, uric acid, and calcium show changes similiar to that of the urea nitrogen.

TABLE 6.—HOURLY OUTPUT OF URINE AS INFLUENCED BY PITUITARY SOLUTION WHEN WATER WAS FORCED—150 C.C. EVERY HALF HOUR FROM 6 A. M. TO 6 P. M., AND WHEN UREA WAS FORCED, 1.6 GM. EVERY HOUR FROM 6 A. M. TO 6 P. M.; 0.25 C.C. OF PITUITARY SOLUTION INJECTED AT 10:45 A. M.

Time	Vol.	Sp. Gr.	Urea N		NaCl		Creatinin		Uric Acid		Calcium		Acidity	
			%	Gm.	%	Gm.	Mg.*	Mg.	Mg.*	Mg.	Mg.*	Mg.	Per 100	Total
6- 7 a.m.	305	1.005	0.14	0.42	0.19	0.58	7.8	24	7.7	23	3.7	11.0		
7- 8 a.m.	330	1.004	0.15	0.49	0.17	0.56	6.9	23	7.4	25	2.4	8.2	1.2	3.9
8- 9 a.m.	195	1.005	0.20	0.38	0.10	0.20	8.3	16	10.0	20	2.7	5.3	3.3	6.4
9-10 a.m.	300	1.003	0.15	0.46	0.037	0.11	6.2	19	7.2	21	1.3	3.9	1.1	3.4
10-11 a.m.	205	1.004	0.23	0.46	0.056	0.12	15.0	30	11.0	23	1.6	3.3	1.9	3.9
11-12 a.m.	36	1.019	1.10	0.40	0.18	0.062	46.0	17	44.0	16	4.9	1.8	4.8	1.7
12- 1 p.m.	45	1.019	1.29	0.58	0.14	0.063	45.0	20	39.0	18	4.7	2.1	13.1	5.9
1- 2 p.m.	45	1.020	1.14	0.51	0.13	0.057	43.0	19	34.0	15	0.8	0.4	6.2	2.8
2- 3 p.m.	56	1.016	0.76	0.43	0.052	0.029	25.0	14	21.0	12	1.1	0.6	3.1	1.8
3- 4 p.m.	64	1.008	0.55	0.36	0.025	0.016	19.0	12	13.0	8.3	1.1	0.72	3.5	2.2
4- 5 p.m.	270	1.006	0.25	0.68	0.022	0.059	8.3	22	6.2	17	1.6	4.5	2.3	6.2
5- 6 p.m.	300	1.004	0.36	1.07	0.019	0.057	5.9	18	5.4	16	2.9	8.7	2.4	7.1
Day.....	2,156	.....	0.29	6.27	0.089	1.91	10.9	234	10.0	214	2.3	50.5	2.4	45.0
Night.....	2,385	1.001	0.23	5.41	0.028	0.68	9.3	220	6.3	150	2.9	69.0	2.4	58.0
Total.....	4,541	.....	0.26	11.68	0.061	2.79	10.0	454	8.1	364	2.6	119.5	2.3	103.0

* Milligrams per 100 c.c.

On the second day, 1.6 gm. of pure urea (0.75 gm. urea nitrogen) were given in water every hour from 6 a. m. to 6 p. m. The urea was eliminated at an almost constant rate of 0.44 gm. of urea nitrogen per hour. This rate is scarcely affected by the injection of pituitary solution. The chlorid elimination is large in the first hour and thereafter sinks rapidly. The phenomenon, observed also on the following day, is known as the "morning flush." The sinking is not greatly accelerated by pituitary solution, possibly because the level is already low. The creatinin and the uric acid output show little change; the calcium output is diminished.

On the third day, no urea or sodium chlorid was added to the diet. There is very little effect of pituitary solution on elimination of chlorid or urea, both these substances being present only in low concentrations in the urine.

Study was made of acid elimination by the urine on the last two days. The number of cubic centimeters of tenth normal sodium

TABLE 7.—HOURLY OUTPUT OF URINE AS INFLUENCED BY PITUITARY SOLUTION WHEN WATER WAS FORCED—150 C.C. EVERY HALF HOUR FROM 6 A. M. TO 6 P. M., AND WHEN ACID SODIUM PHOSPHATE WAS GIVEN, 1 GM. EVERY HOUR FROM 6 A. M. TO 6 P. M.; 0.25 C.C. PITUITARY SOLUTION INJECTED AT 10:30 A. M.

Time	Vol.	Sp. Gr.	Urea N		NaCl		Creatinin		Uric Acid		Calcium		Acidity	
			%	Gm.	%	Gm.	Mg.*	Mg.	Mg.*	Mg.	Mg.*	Mg.	Per 100	Total
6- 7 a.m.	670	1.001	0.12	0.83	0.083	0.56	7.4	50	7.6	50.0	5.4	36.0	2.4	16.0
7- 8 a.m.	280	1.003	0.081	0.23	0.085	0.24	8.6	24	7.3	20.0	4.0	11.0	3.2	8.9
8- 9 a.m.	100	1.002	0.11	0.17	0.040	0.064	12.0	18	8.8	14.0	5.3	8.5	11.0	17.0
9-10 a.m.	170	1.002	0.12	0.20	0.020	0.032	12.0	21	8.5	15.0	6.0	10.0	11.8	20.0
10-11 a.m.	65	1.006	0.16	0.10	0.031	0.031	23.0	15	16.0	10.0	8.0	5.0	27.0	18.0
11-12 a.m.	31	1.014	0.44	0.14	0.048	0.015	60.0	18	11.0	3.1	40.3	13.0	58.0	18.0
12- 1 p.m.	41	1.017	0.48	0.20	0.030	0.012	47.0	19	7.9	3.2	26.0	11.0	69.0	28.0
1- 2 p.m.	42	1.015	0.40	0.17	0.024	0.010	42.0	18	6.3	2.6			51.0	20.0
2- 3 p.m.	49	1.013	0.32	0.16	0.015	0.007	37.0	18	4.1	2.9			55.0	27.0
3- 4 p.m.	67	1.006	0.17	0.12	0.016	0.011	22.0	15	2.6	4.5			34.0	23.0
4- 5 p.m.	243	1.005	0.10	0.24	0.010	0.024	10.0	25	1.2	4.1			17,0	42.0
5- 6 p.m.	325	1.005	0.059	0.19	0.009	0.029	6.2	20	1.5	4.8			10.0	33.0
Day.....	2,143	.....	0.13	2.75	0.049	1.04	12.2	261	6.2	133.0			12.3	271.0
Night.....	2,060	1.003	0.063	1.30	0.011	0.22	8.9	183	1.9	39.0			1.2	246.0
Total.....	4,203	.....	0.096	4.05	0.030	1.26	10.5	444	8.1	172.0			12.1	517.0

* Milligrams per 100 c.c.

hydroxid required to neutralize the urine is indicated in the last column of the tables. On the third day 1 gm. of acid codium phosphate was given every hour from 6 a. m. to 6 p. m. As is seen, the "acidity" of the urine is much greater on this day. There is little if any diminution of acid elimination following the injection of pituitary solution.

Unfortunately, the patient left the hospital before further studies could be made.

SUMMARY

1. Study is made of the urinary output of a 9½ year old boy suffering from diabetes insipidus, as influenced by injections of pituitrin.

2. Following injections of from 0.25 to 1 c.c. of surgical pituitrin, there is a marked diminution of the urine volume.

3. This diminution persists for from 5 to 6 hours, sometimes much longer.

4. The volume of night urine is reduced when pituitrin is injected at any time on the preceding day.

5. The hourly rate of elimination of chlorids is always reduced after injections of pituitary solution.

6. The hourly rate of elimination of urea is usually only slightly, if at all, reduced by injection of pituitary solution.

7. The hourly rates of elimination of creatinin and uric acid are only slightly reduced by injection of pituitary solution.

8. The hourly rate of elimination of titratable acids in the urine is only slightly influenced by these injections.

9. The hourly rate of elimination of no substance studied is increased by injections of pituitary solution.

10. When the hourly ingestion of water and sodium chlorid or urea is maintained at a constant high level, the urea elimination is quite uninfluenced by the injection of pituitary solution, whereas, the chlorid elimination is considerably diminished, and the water elimination very much diminished.

11. Pituitrin injections in diabetes insipidus control urine output primarily and thirst secondarily.

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